

Study of Oxidative Stress and Inflammatory Status in Thyroid Dysfunction: A Systematic Review

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ABSTRACT

Background: The frequency of thyroid disorders is rising quickly, making them a major socioeconomic issue. Oxidative stress is also connected to thyroid disorders with increasing frequency. Moreover, an association between underlying inflammatory processes and oxidative damage must be considered because most thyroid ailments are seen to have an underlying inflammatory basis.

Aim & objectives: This systematic review assesses the oxidative stress in thyroid dysfunctions and their association with inflammatory processes.

Methodology: A systematic review of the literature was done using databases that included- PubMed, Scopus, Science Direct, Research Gate and Google Scholar using the keywords “oxidative stress”, “inflammatory markers,” and “thyroid disorders” from 2000-2022. After separately evaluating citations and abstracts, two reviewers examined full-text publications and came to an agreement on the research that should be included. We conducted this research using the preferred reporting items for systematic research and meta-analysis (PRISMA).

Results: A total of 531 articles were found, out of which only 51 met the criteria of inclusion. A significant heterogeneity across the studies was found. In these studies, various oxidant/antioxidant and inflammatory markers were used to determine oxidative stress and its association with inflammatory processes. Most studies found a high level of reactive oxygen species (ROS) induced by an imbalance of thyroid hormones that can cause oxidative stress with a consequent lipid peroxidation response and accelerated inflammatory response.

Conclusion: Data from the literature demonstrated a significant correlation between oxidative damage results and elevated ROS production. Thyroid issues can potentially trigger or exacerbate oxidative stress and ROS generation, which can worsen oxidative damage. Additionally, recent research indicates that OS and inflammation may be related in some way since mitochondrial reactive species are signalling molecules that cause the release of proinflammatory cytokines.

Keywords: Thyroid dysfunction, Oxidative stress, Inflammatory markers, Antioxidants.

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INTRODUCTION

The thyroid gland is the body's largest endocrine organ, specialized to perform various functions. Its role is to secrete thyroid hormones, such as tetraiodothyronine (T4) and less triiodothyronine (T3). The rates of cellular respiration and metabolism in almost every kind of mammalian cell are largely regulated by thyroid hormones (THs).¹ The rise in the rates of both catabolic and anabolic processes is part of the broader metabolic effects of THs, which include a relative acceleration of basal metabolism.² The impact of thyroid hormones on cellular respiratory rate can be explained by its capability to alter the amount and working of mitochondrial respiratory chain constituents in many ways, which may lead to a rise in

the production of reactive oxygen species (ROS) and other toxic metabolites. “Oxidative stress” describes a condition of damage caused by ROS. An imbalance between the body's synthesis of prooxidant chemicals and its antioxidant defense system is referred to as oxidative stress.³

ROS production could play important functions in many cells like leukocytes and endothelial and mesangial cells.⁴ Dual oxidases (DUOX) are enzymes essential for the production of hydrogen peroxide and they are crucial for thyroid peroxidase (TPO), which catalyzes thyroid hormone production.⁵ DUOX1 and DUOX2 are from the oxidases family which are involved in thyroid hormone synthesis. They are the maturation factors that enable dual oxidase enzymes to translocate to the follicular

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cell membrane, which boosts their enzymatic impact. Typically, they function in tandem with DUOX1 and DUOX2. The human thyroid gland's intracellular ROS-generating mechanism is the recently identified enzyme NADPH oxidase 4 (NOX4).⁶

Thyroid epithelial cells naturally create modest levels of ROS, which are crucial for the formation of thyroid hormone.⁷ They are not always harmful because of constantly detoxified during hormone production or by endogenous antioxidant mechanisms. In overwhelming quantities, they may be toxic and have been seen to be connected to inflammation and degradation of cells.⁸ Because thyroid hormones are involved in cellular metabolism and oxygen consumption, they are believed to significantly affect oxidative stress. The endocrine negative feedback system in the body regulates them to stay within normal ranges. However, variations in their concentrations may modify the redox environment by influencing the quantity and activity of components in the mitochondrial respiratory chain, leading to a rise in ROS production, which is frequently shown to be suppressed by antioxidants. When ROS are produced excessively, thyroid hormones enhance oxygen consumption. This throws off the prooxidant/antioxidant balance, causing oxidative stress and subsequent damage to DNA, lipids, proteins, and cellular structures.⁹

Different defense mechanisms against free radical generation have been classified in different cellular locations, including the cytosol, the ER, mitochondria, and the cell membrane. Some enzymes and transition metal binding proteins of are thought to inhibit or at least prevent the generation of free radicals.¹⁰

Additionally, thyroid hormones usually target mitochondria. There is a continuous flow of oxygenated water during thyroid hormone synthesis, which is required for iodine intrafollicular oxidation in the presence of thyroid peroxidase (TPO).¹¹ The potential link between reactive oxygen species and dysfunctional thyroid gland function has been under attention in recent years, but concrete evidence is still needed. Moreover, an association between underlying inflammatory processes and oxidative damage also needs to be considered because most of the thyroid ailments are seen to have an underlying inflammatory basis.

MATERIAL AND METHODS

Search Strategy

To study the oxidative damage and inflammatory status in patients with thyroid disease, a systematic review search was done in the databases of PubMed, Scopus, Research Gate, Science Direct and Google Scholar for the period 2000 to 2022. The search words used in the database are “oxidative stress” “thyroid disorders” or “inflammatory markers” using Boolean operators. Additional articles were identified through a review of cross-references to expand the search. The preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines were followed in conducting the systematic review.

Inclusion Criteria

- All articles must include any one of the thyroid diseases.

- Articles dealing with thyroid dysfunction with oxidative stress
- Papers analyzing thyroid dysfunction and its association with inflammatory markers
- Articles retrieved only from reliable web search engines

Exclusion Criteria

- Studies not within the field of interest of this review
- Literature not available in the English language
- Criticism was also avoided

Study Selection and Analytical Process

Studies investigating oxidative stress, inflammation and their association with thyroid dysfunction were eligible for inclusion in this review. Two different reviewers reviewed all the articles included at different times. If any conflict occurred between the two, a third reviewer was also involved to comment on the included literature. Articles were rejected if they were ineligible. Hence, all the types of biases were completely eliminated. The standards defined by the PRISMA were used to investigate the collected publications.

Literature Search

A summary of the literature search process is shown in Figure 1. The comprehensive net literature search from PubMed/MEDLINE, Science Direct, Scopus and Google Scholar databases revealed 531 records. Among these records, 480 were excluded and 51 were selected and retrieved in full-text versions. Further, cross references obtained while screening the main references of the selected articles were also found and those found relevant and appropriate to the topic were included in the present systematic literature review.

RESULTS

The main characteristics of the studies included are summarized chronologically as shown in Tables 1 and 2. A total of 531 articles were found, out of which only 51 met the criteria of inclusion. A significant heterogeneity across the studies

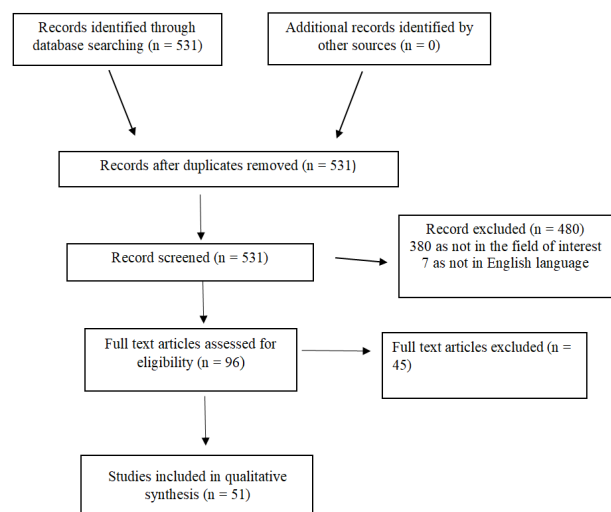


Figure 1: PRISMA flow diagram for updated systematic review including searches from various databases

Table 1: depicting studies related to the oxidant and antioxidant status in thyroid dysfunction patients from 2000-2022.

S. No.	Authors	Publication year	Sources of article	Parameters	Outcomes
1	Eddib I, <i>et al.</i>	2022	Science Direct	Free thyroxin 4 (FT4) thyroid stimulating hormone (TSH), malondialdehyde (MDA), glutathione peroxidase (GPx), superoxide dismutase (SOD) and glutathione (GSH).	Lipid peroxidation is elevated in hypo- and hyperthyroidism. Thyroid patients' decreased glutathione levels and increased GPx activity ¹²
2	Roshni R, <i>et al.</i>	2021	Scopus	oxidative stress index (OSI), Paraoxonase-1 (PON-1), and thyroid profile	OSI and TOS increase whereas no change in the antioxidant status as well as PON-1 activity in SCH patients ¹³
3	Kochman J, <i>et al.</i>	2021	PubMed	Review article to investigate oxidative damage in thyroid dysfunction and diseases	This study suggested the potential link between oxidative stress and thyroid diseases ¹⁴
4	Sultana R, <i>et al.</i>	2021	PubMed	MDA, TAC	The mean MDA level was lower but TAC was significantly increased in hyperthyroid patients ¹⁵
5	Szczepanik J, <i>et al.</i>	2021	PubMed	Zn, Cu, FRAP, TBARS, total phenolics	No difference in Cu, Zn and FRAP levels while higher levels of TBARS concentration in Hashimoto's thyroiditis women ¹⁶
6	Sankha S, <i>et al.</i>	2021	Google Scholar	MDA, protein carbonyl (PCO), GSH, SOD, GPx, catalase and SOD-to- (GPx+ CAT) ratio	High levels of MDA and PCO while, reduced levels of GSH, SOD, SOD/(GPx+ CAT) ratio were observed in hypothyroid patients than controls. ¹⁷
7	Mahmood AS, <i>et al.</i>	2020	Scopus	CAT, SOD, and GR	CAT, SOD, and GR were significantly increased in hyperthyroidism whereas decreased in hypothyroidism ¹⁸
8	Rabbani E, <i>et al.</i>	2020	PubMed	Thyroid profile, oxidative markers (MDA, TAC)	Anthropometric indices and TAC levels were decreased in hypothyroid patients ¹⁹
9	Ates I, <i>et al.</i>	2018	PubMed	TOS, OSI	TOS and OSI levels were raised in while, paraoxonase-1 and arylesterase did not show any difference in overt hypothyroid patients compared with controls. ²⁰
10	Kalpana P, <i>et al.</i>	2017	Google Scholar	Lipid profile, TBARS, vitamin E, vitamin C, iron, phosphorus	TC, LDL-C, VLDL, TGs, and FFA levels were elevated while HDL-C, minerals (iron, phosphorus) and vitamins (A, E) levels were reduced and serum lipid peroxidation was raised in hypothyroidism compared to controls. ²¹
11	Deraz HA, <i>et al.</i>	2016	PubMed	MDA, SOD, CAT, TAC, lipid profile, thyroid profile	High levels of TSH, TC, TGs, LDL-C, catalase, SOD and MDA whereas low levels of HDL-C and TAC were found in both overt and subclinical hypothyroidism. ²²
12	Kaur A, <i>et al.</i>	2016	Science Direct	Thyroid profile, lipid profile, TAS	The levels of S. Cholesterol, TG, VLDL-C, and LDL-C were elevated and the difference was nonsignificant while the levels of S. HDL-C were lowered. Serum TAS levels were decreased in hypothyroid patients. ²³
13	Ates I, <i>et al.</i>	2015	PubMed	TAS, TOS, OSI, total thiol, arylesterase	TOS and OSI were elevated whereas no significant changes in paraoxonase-1 and arylesterase were observed in overt hypothyroid than in controls. ²⁴
14	Baser H, <i>et al.</i>	2015	PubMed	TAS, TOS, ox-LDL	TAS level was decreased while TOS level was elevated in autoimmune thyroiditis patients but ox-LDL was not significantly change. ²⁵
15	Cheserek MJ, <i>et al.</i>	2015	PubMed	MDA, advanced oxidation protein products (AOPP), TAC	MDA level was higher in SCH while, AOPP and TAC were not significantly changed compared to controls. ²⁶
16	Naazeri S, <i>et al.</i>	2014	ResearchGate	TAC, catalase, SOD	TAC reduced in hyperthyroidism but no change was observed in hypothyroidism while, catalase and SOD activity increased in hypo-and hypothyroidism compared to healthy controls. ²⁷
17	Haribabu A, <i>et al.</i>	2013	ResearchGate	MDA, protein carbonyl (PCO)	Increased MDA, PCO levels were found in OHT and SHT. ²⁸

18	Reddy VS, <i>et al.</i>	2013	Science Direct	MDA, GSH, TAC as the ferric reducing ability of plasma (FRAP), SOD, GPx, SOD/GPx ratio and catalase	n both overt and subclinical hypothyroid individuals, MDA and GPx values were greater while GSH, FRAP, SOD, and SOD/GPx values were lower. However, there was no change in the activities of CAT and GR compared to a healthy individual. ²⁹
19	Rostami R, <i>et al.</i>	2013	PubMed	Thyroid profile, GSH, GPx, GR, GGT	Mean UIE and GPx levels were higher while, GSH level was lower in Hashimoto's thyroiditis compared to controls. No change in GR and GGT activity was found. ³⁰
20	Cebeci E, <i>et al.</i>	2012	PubMed	Oxidative stress index, paraoxonase, arylesterase	In subclinical hypothyroidism PON and ARE activity reduced while OSI was higher than controls. ³¹
21	Santi A, <i>et al.</i>	2012	PubMed	Lipid profile, TBARS, catalase, SOD, and arylesterase	TC, LDL-C, TBARS and CAT were elevated and arylesterase activity was reduced in subclinical hypothyroidism while, SOD did not change as compared to control groups. ³²
22	Naazeri S, <i>et al.</i>	2012	ResearchGate	TAC, catalase, SOD	TAC decreased in hyperthyroidism but no change was observed in hypothyroidism. Catalase and SOD levels were raised in both hypo- and hyperthyroidism ³³
23	Haribabu A, <i>et al.</i>	2012	PubMed	MDA, protein carbony (PCO)	Increased in the levels of MDA and PCO in OHT and SHT groups compared to controls was observed ³⁴
24	Wang D, <i>et al.</i>	2011	PubMed	TAS, TOS, OSI	In individuals with thyroid cancer, TAS levels dropped while TOS and OSI were greater. ³⁵
25	Santi A, <i>et al.</i>	2010	PubMed	Lipid profile, TBARS, SOD, catalase, vitamin E	TC, LDL-C, TGs, TBARS, SOD, catalase, and vitamin E concentration were elevated in overt hypothyroidism. ³⁶
26	Torun AN, <i>et al.</i>	2009	PubMed	MDA, TAS, lipid profile	The elevated level of MDA was observed in both subclinical and overt hypothyroidism while, TAS showed no significant change between these two groups. ³⁷
27	Coria MJ, <i>et al.</i>	2009	PubMed	TBARS, nitric oxide, paraoxonase	TBARS and PON-1 activity did not show any changes between overt hypothyroid, subclinical hypothyroid and euthyroid women. Levels of NO were elevated in OHT but not in SHT compared to ET. ³⁸
28	Erdamar H, <i>et al.</i>	2008	PubMed	MDA, nitrite vitamin E, myeloperoxidase	In hypothyroid patients, raised levels of MDA, nitrite, vitamin E, and myeloperoxidase activity were noted; in hyperthyroid patients, elevated levels of malondialdehyde and myeloperoxidase activity were noted. ³⁹
29	Baskol G, <i>et al.</i>	2007	PubMed	MDA, paraoxonase, nitric oxide, superoxide dismutase	MDA and NO levels were higher and PON1 was lower while SOD activity was not found different in hypothyroid patients than in controls. ⁴⁰
30	Venditti P, <i>et al.</i>	2006	PubMed	Review article	The major target of oxidative stress, the mitochondria, may be responsible for tissue dysfunction associated with hyperthyroidism. ⁴¹
31	Lampka M, <i>et al.</i>	2006	PubMed	OxLDL, SOD, TAS	MDA activity was increased whereas anti-oxLDL, TAS, and SOD levels showed no difference in hyperthyroid patients than healthy individuals. ⁴²

was found. In these studies, various oxidant/antioxidant and inflammatory markers were used to determine oxidative stress and its association with inflammatory processes. Most studies found a rise in ROS induced by an imbalance of thyroid hormones that can ultimately result in oxidative stress with a consequent lipid peroxidation response and accelerated inflammatory response.

DISCUSSION

Several investigations have shown a substantial variation in T3, T4, and TSH levels in the various thyroid oxidative stress conditions. As a result, oxidative stress development is significantly influenced by thyroid hormones.⁴⁹ The

metabolism of many cell in the body may be targeted, influenced, or changed by thyroid hormones because they speed up cellular reactions and boost oxidative metabolism. Oxidative stress develops when free radicals are generated excessive and the antioxidant defence system is ineffective [50]. Unscavenged free eventually damage vital cell components including DNA, proteins, and membrane-bound lipids. Each cell has a defence mechanism to counteract the consequences of free radical generation through DNA repair enzymes and/or antioxidants. MDA is formed as a result of lipid peroxidation.⁵¹ If pro-oxidants and oxidative stress are not effectively controlled, they can cause many chronic and degenerative diseases, aging, and pathologies. An imbalance in thyroid

Table 2: depicting Studies related to the inflammatory status in thyroid dysfunction patients

S. No.	Authors	Publication year	Sources of article	Parameters	Outcomes
1	Suzan S, <i>et al.</i>	2021	Scopus	Hs-CRP, lipid profile, Osteopontin (OPN)	The serum concentration of Hs-CRP, TC, TGs, LDL-c, VLDL-c and osteopontin (OPN) was increased in hypothyroid patients. ⁴³
2	El- Hefnawy KA, <i>et al.</i>	2019	Google Scholar	CRP, interleukin (IL)-6, IL-10, lipid profile	Increased levels of CRP, IL-6, and IL-10 in subclinical hypothyroid patients. ⁴⁴
3	Ahmad N, <i>et al.</i>	2018	Google Scholar	Hs-CRP	Hs- CRP activity raised in the thyroid dysfunction patients. ⁴⁵
4	Savas E, <i>et al.</i>	2016	PubMed	Pro-calcitonin (PCT), C-reactive protein (CRP), mean platelet volume (MPV), and erythrocyte sedimentation rate (ESR)	ESR, CRP, and PCT were raised while MPV was reduced in both hypo and hyperthyroidism. ESR, and PCT levels were raised in autoimmune and non-autoimmune disorder patients whereas MPV decreased in hypothyroidism, hyperthyroidism, and non-autoimmune patients than controls. ⁴⁶
5	Marchiori RC, <i>et al.</i>	2015	PubMed	Thyroid profile, Hs CRP, Tumor necrosis factor alpha (TNF-α), interleukin 1, IL-10, TBARS, aminolevulinic acid dehydratase(δ-ALA-D) and lipid profile	Increased levels of IL-10 and decreased levels of IL-1, and TNF-α while, no significant difference in hs-CRP was observed in hypothyroid patients ⁴⁷
6	Gupta G, <i>et al.</i>	2015	Google Scholar	Lipid profile, ESR, CRP, interleukin-6	TC, TGs, and LDL-C were higher while HDL-C was lower in the subclinical hypothyroid compared to the euthyroid group. TSH level was positively associated with inflammatory markers in subclinical hypothyroid patients. ⁴⁸

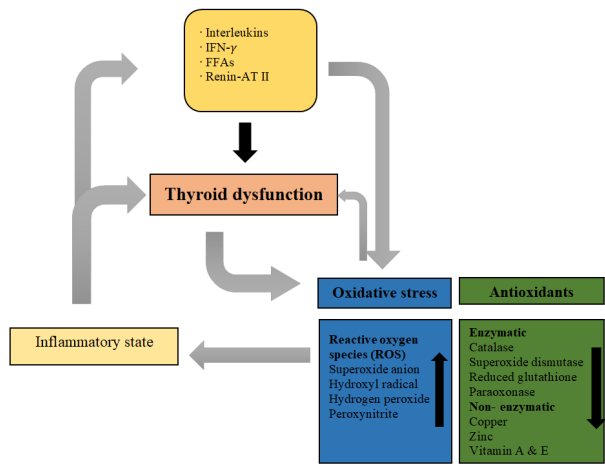


Figure 2: Vicious cycle

hormones causes hypothyroidism and hyperthyroidism, which leads to formation of ROS and the consequent need for antioxidants.⁵² Free radical formation and lipid peroxide levels rise in proper to the severity of hyperthyroidism leading to accelerated metabolic rate. Conversely, redox potential failure in chronic hypothyroidism sets off a series of events that cause free radicals production and the metabolic suppression of antioxidant capacity. The increased generation of free radicals in the ETC of the mitochondrial inner membrane may be the cause of the observed antioxidant deficiency in hypothyroidism.⁵³

The onset and course of several diseases have been related to oxidative stress. Researchers suggest that the oxidative/anti-

oxidative system was not in balance in both hyperthyroidism and hypothyroidism. This imbalance might be brought on by changes in metabolic rates that cause excessive levels of nitric oxide, hydrogen peroxide (H₂O₂), and other ROS. Free radical overproduction causes tissue damage and inflammation, which in turn triggers the onset of related disorders. The majority of recent researches have observed that oxidative stress levels have risen in peripheral blood in thyroiditis due to various etiologies consequent to the decreased cellular ability to scavenge reactive oxygen species.¹²

Numerous studies have also shown that, independent of the type of thyroid dysfunction, there are substantial changes in the levels of inflammatory markers in autoimmune, non-autoimmune, hypothyroid, and hyperthyroid diseases. This confirms the significance of inflammation has role in the development of thyroid dysfunctions.⁴⁶ There may be two approaches to describe how inflammation might increase oxidative stress. Firstly, inflammation may raise the quantity of H₂O₂ in thyroid epithelial cells. Secondly, inflammation may causes T and B lymphocytes to activate the NADPH oxidase (NOX) enzyme, which may raise the production of ROS.⁵⁴

In addition to inflammatory processes, hormonal imbalances can also have a negative relationship with OS. Hormones generally regulate the normal generation of antioxidants which keeps oxidative stress to a minimum. OS is thus, connected to both hormonal imbalance and systemic inflammation. Heterogenous in vitro and in vivo investigations have shown that thyroid hormones are crucial in the regulation of a fine balance between antioxidant and prooxidant levels.¹⁰ Interestingly, deiodinases are the enzymes that convert T4 into

T3 peripherally, as well as antioxidant enzymes like GP, both depend on reduced glutathione (GSH), an essential cofactor. Prior research has demonstrated that both hypothyroidism and hyperthyroidism, as well as the acute or chronic nonthyroidal disease syndrome whether with autoimmune or non-autoimmune basis, are found to be related to OS.⁵⁵

Total antioxidant status (TAS) and total oxidant status (TOS) are indicators of the system's overall redox balance. According to Ates I, *et al.* concentrations of TAS, TOS, and OSI were examined between individuals with Hashimoto's disease, euthyroidism, overt and subclinical hypothyroidism, and controls. As a consequence of their research, they found that TAS reduced and that TOS and OSI considerably rose during the disease's various stages.²⁵

According to Borowska, *et al.* the amount of zinc in blood serum is lower in those who have Hashimoto's thyroiditis. This may be due to the thyroid gland chronic inflammation or to an inadequate intake of zinc through diet. The biological activity of free T3 and T4 depends on zinc (as do selenium and iodine), and their metabolic activity is adversely impacted by zinc deficiencies.²⁴

A study by Hamed A. Deraz, *et al.* revealed that in both overt and subclinical hypothyroidism patients had significantly elevated concentrations of total cholesterol, TGs and LDL but a reduced level of HDL as compared to controls. Raised concentrations of total cholesterol and LDL seen in hypothyroidism may be due to various alterations in the production and metabolism of lipids. Thyroid hormones specifically T3 help to induce the HMG-CoA reductase and it is the very 1st step in the biosynthesis of cholesterol.⁵⁶ They also help in the regulation of LDL cholesterol receptors which start the uptake of LDL-C which is rich in cholesterol by directly attachment to particular thyroid hormone-responsive elements.⁵⁷

After examining the linked between thyroid autoantibodies and OS indicators, a negative association of TAS level was found with anti-TG and anti-TPO, however, a positive association of TOS was found with anti-TG in the research by Baser *et al.*²⁵ The oxidant compounds like malondialdehyde (MDA) and protein carbonyl were observed to positively correlate with anti-TPO levels, according to Nanda *et al.*⁴³ GSH and anti-TPO had shown a negative correlation in the research of Rostami *et al.* By using a linear regression analysis, it was shown in the study by Ihsan Ates, *et al.* that the indicators of oxidative stress were shown to be impacted by hypothyroidism, which proclaims that OS is associated with thyroid hormone deficit, which is caused by enhanced auto-immunity and inflammation, or both.²⁵

Thus, it can be emphasized that inflammation, oxidative stress and thyroid dysfunction are all interconnected, supporting a model proposed by Antonio Mancini, *et al.* also holds good. Inflammation impacts thyroid function by altering hormone and cytokine levels, which may result in enhanced oxidative stress and can result in nonthyroidal illness syndrome or pituitary thyroid axis depression resulting in overt thyroid dysfunction. When hypothyroidism increases oxidative stress,

which in turn exacerbates hypothyroidism by inhibiting deiodinases, a vicious cycle is established at the tissue level (Figure 2). The possible reason behind the blockage of the function of deiodinases might be due to the consumption of GSH in scavenging oxidant species generated due to increased OS. Thyroid hormones can thus, act as antioxidant regulators and be protective against OS.¹⁰

IMPLICATIONS OF THE PRESENT SYSTEMATIC REVIEW

Policy Implications

In this research, various validated publications have been reviewed and assessed. To ascertain the reliability and accuracy of various aspects of current evidence available, the study's authors have investigated and critically appraised various monitoring systems. The methods adopted were thoroughly examined and the outcomes obtained from various studies were synthesized together to arrive at meaningful and practically applicable conclusions.

FUTURE IMPLICATIONS

As included in this systematic review following may be the future implications of this study:

- Improvement in the oxidant/antioxidant balance may result in improvement in the prognosis of thyroid dysfunction patients.
- Improved prognosis in these patients may further lead to the minimization of long-term complications resulting in improvement in overall quality of life in thyroid dysfunction patients.
- Administration of antioxidants along with thyroid medications may improve overall outcomes in such patients.
- The knowledge synthesized from this study may pave the way for further studies in longer sample size with even more antioxidant, oxidant, and inflammatory parameters.

LIMITATIONS

In this systematic review article, only a limited number of articles could be included and were analyzed and only a few prospective and follow-up studies could be incorporated in the study. Most importantly, significant heterogeneity was found across various studies which hampered the building up of firm the association between underlying inflammatory processes and oxidative stress in thyroid dysfunction. Lastly, the majority of the research included in our study was conducted at a single-centre. Hence, high-quality prospective multi-centric studies need to be evaluated further.

CONCLUSION

Data from previous literature indicates that a multitude of mechanisms may be involved in the development of thyroid pathologies, consequent to which may result in a wide assay of thyroid diseases. Thyroid diseases may be caused by aberrant control of antioxidant enzymes and enhanced generation of pro-oxidants and ROS in hypo- and hyperthyroid states.

Various research suggests that thyroid levels and oxidative stress have an intricate connection. Recent study indicates that mitochondrial reactive species may function as signalling molecules and mediate the production of proinflammatory cytokines, which further supports the link between OS and inflammation.

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