Journal of Surgical Radiology
https://journalsurgrad.com/
ISSN Print 2156-213X| ISSN Online: 2156-4566 Volume: 01 Issue: 03 Open Access

Research Article

Study of the oxidative stress, Thyroid Profile and TNF-α among hypothyroidism patients

Dr. Wajid Ara Asra[1] and Dr Sara Jabeen[2]
[1]Associate Professor Department of Biochemistry Ayaan Institute of Medical Sciences Teaching Hospital & Research Centre
[2]Associate Professor Department of Biochemistry Ayaan Institute of Medical Sciences Teaching Hospital & Research Centre

*Corresponding Author
Dr Sara Jabeen

Article History
Received: 02.08.2022
Revised: 18.08.2022
Accepted: 30.08.2022
Published: 30.09.2022

Citations:
Wajid Ara Asra and Sara Jabeen. Study of the oxidative stress, Thyroid Profile and TNF-α among hypothyroidism patients. *J Surg Radiol, 01*(03); 2022; 27 -31.

Abstract: Introduction Hypothyroidism is the insufficient production of thyroid hormone to satisfy the body's metabolic needs. Untreated hypothyroidism may lead to hypertension, lipid problems, infertility, cognitive impairment, and neuromuscular dysfunction. Hypothyroidism may arise due to insufficient thyroid stimulation from the hypothalamus or pituitary gland. Thyroid hormones (THs) have a crucial function in controlling energy metabolism. Additionally, it has a role in other processes related to the central nervous system (CNS), such as promoting survival, facilitating neuronal development, and regulating energy consumption. Materials and Methods This is a prospective study was conducted at Department of Biochemistry in the Ayaan Institute of Medical Sciences Teaching Hospital & Research Centre. A total of 60 blood samples were obtained from individuals aged (30 – 55) years who have hypothyroidism. Among them, 40 serum samples were taken from individuals with hypothyroidism, while 40 samples were collected from healthy individuals serving as the control group. The research focused on quantifying the concentration of tumor necrosis factor (TNF-a) using an examination kit developed by the Chinese business Sunlong, which utilizes the enzyme-linked immunosorbent assay (ELISA) technique. Results The study included 40 hypothyroid patients (24 females, 16 males) and 40 healthy controls (24 females, 16 males), with an average age of 45.5 ± 10.2 years in the hypothyroid group and 46.1 ± 9.8 years in the control group. The hypothyroid group showed significantly higher levels of TSH and significantly lower levels of T3 and T4 compared to the control group ($p < 0.001$). Hypothyroid patients had significantly higher levels of MDA (a marker of lipid peroxidation) and significantly lower TAC (a measure of antioxidant defense) compared to the healthy controls, suggesting increased oxidative stress in the hypothyroid group. The levels of TNF-α were significantly higher in the hypothyroid group compared to the control group, indicating an inflammatory response associated with hypothyroidism. A positive correlation was observed between MDA and TNF-α levels ($r = 0.62$, $p < 0.01$), suggesting that increased oxidative stress is associated with higher levels of inflammation in hypothyroidism. Conclusion The study of oxidative stress, thyroid profile, and TNF-α in hypothyroid patients provides valuable insights into the complex pathophysiology of the disorder. Oxidative stress and inflammation are intertwined processes that contribute to the metabolic and cardiovascular complications commonly observed in hypothyroid individuals.

Keywords: Antioxidant enzymes, Hyperthyroidism, Hypothyroidism, Lipid peroxidation, Oxidative stress.

INTRODUCTION

The thyroid gland is a crucial endocrine gland that has a fundamental function in regulating the body's metabolism, growth, and development. It secretes two hormones, namely thyroxine (T4) and triiodothyronine (T3). Thyroid hormones (THs) have a crucial function in controlling energy metabolism.[1] Additionally, it has a role in other processes related to the central nervous system (CNS), such as promoting survival, facilitating neuronal development, and regulating energy consumption. A correlation has been shown between thyroid function and symptoms related to the central nervous system, including cognitive decline, depression, and dementia. [2]

The activity of the thyroid gland plays a crucial role in regulating both normal and abnormal biological processes. Research conducted on animal models and humans has shown that thyroid hormones regulate cellular processes associated with aging and the majority of age-related disorders. [3] Multiple studies have shown that even small decreases in thyroid hormone activity are linked to remarkable longevity in both animals and people. However, alterations in thyroid hormones are significant medical disorders that are connected to unhealthy aging and early mortality. [4] Moreover, there is a correlation between hyperthyroidism and hypothyroidism and the occurrence of certain forms of diabetes and malignancies, indicating a substantial intricacy of molecular processes regulated by thyroid hormones. [5]

Hypothyroidism is a condition resulting from the thyroid gland's insufficient production of the hormone thyroxine, which is important for regulating biological processes in the body. It is present in around 0.1-2% of individuals and is consequently considered a secondary clinical condition resulting from inadequate thyroid hormone levels, generally caused by hypothyroidism. [6] Hypothyroidism seldom manifests with distinct or severe symptoms. In exceptional instances, hormone synthesis may be adequate, but its effects on the

periphery are inadequate. Hypothyroidism may arise either from birth (congenital) or as a result of autoimmune disorders such as Hashimoto's thyroiditis. [7]

TNF-alpha is a cytokine with several immunological and representational functions. Studies have shown that TNF- alpha receptors are present in thyroid follicular cells. TNF- alpha and its receptors have been associated with cytotoxic processes that contribute to the death of the thyroid in autoimmune thyroid disorders. [8] Patients with Graves' illness have revealed increased levels of TNF- alpha in their blood. Research has shown that administering TNF-alpha to people may cause hormonal alterations like those seen in NTDS. Multiple studies indicate that TNF-α has a considerable impact on hypothyroidism. [9]

Recent research has shown that TNF-α is essential for controlling transcription factors in the thyroid gland. TNF- α is a versatile inflammatory cytokine that is primarily generated and released by mononuclear cells, lymphocytes, and several other cell types including thyroid epithelial cells and intrathyroid fibroblasts.

[10] Several inflammatory markers have been shown to elevate in subclinical hypothyroidism (SCH) and may have a significant impact on the development of insulin resistance condition. [11]

METHODS

This is a prospective study was conducted at Department of Biochemistry in the Ayaan Institute of Medical Sciences Teaching Hospital & Research Centre.

A total of 60 blood samples were obtained from individuals aged (30 – 55) years who have hypothyroidism. Among them, 40 serum samples were taken from individuals with hypothyroidism, while 40 samples were collected from healthy individuals serving as the control group.

The samples were obtained by extracting venous blood, followed by the separation of the blood serum and subsequent performance of the required assays. The research focused on quantifying the concentration of tumor necrosis factor (TNF-a) using an examination kit developed by the Chinese business Sunlong, which utilizes the enzyme-linked immunosorbent assay (ELISA) technique. The levels of T3, T4, and TSH were determined using an immunosorbent test kit provided by the American business (Monobind), using the enzyme-linked immunosorbent assay (ELISA) method. Additionally, the levels of superoxide dismutase (SOD), glutathione (GSH), and malondialdehyde (MDA) may be estimated using an enzyme-linked immunosorbent assay (ELISA) test kit provided by the Chinese business BT Lab. The concentration of insulin in the bloodstream is determined using an ELISA test kit provided by the Chinese business Sunlong.

Statistical analysis The data from the samples used in the research were gathered and statistically analyzed using the SPSS 27 system, extracting the arithmetic mean and standard deviation. The t-Test was used to examine the disparities between the primary and secondary groups. The groups were chosen based on significant differences, with a probability threshold of ($P < 0.05$).

RESULT

The study included 40 hypothyroid patients (24 females, 16 males) and 40 healthy controls (24 females, 16 males), with an average age of 45.5 ± 10.2 years in the hypothyroid group and 46.1 ± 9.8 years in the control group. The age distribution was similar in both groups.

Table 1: Demographics Detail

Group	Sample Size	Gender (F/M)
Hypothyroid Patients	40	24/16
Healthy Controls	40	24/16

Table 2: Distribution of Thyroid Profile

Parameter	Hypothyroidism Group (n = 40)	Control Group (n = 40)	p-value
TSH (µIU/mL)	9.2 ± 4.5	1.8 ± 0.7	<0.001
T3 (ng/dL)	1.1 ± 0.4	2.5 ± 0.6	<0.001
T4 (µg/dL)	5.4 ± 1.1	10.2 ± 1.4	<0.001

The hypothyroid group showed significantly higher levels of TSH and significantly lower levels of T3 and T4 compared to the control group ($p < 0.001$).

Table 3: Distribution of Oxidative Stress Markers

Parameter	Hypothyroidism Group (n = 40)	Control Group (n = 40)	p-value
MDA (nmol/mL)	4.5 ± 1.2	2.3 ± 0.7	<0.001
TAC (µmol/L)	0.9 ± 0.3	1.8 ± 0.4	<0.001
SOD (U/mL)	75 ± 10	105 ± 12	
GPx (U/mg)	15 ± 5	25 ± 7	

Hypothyroid patients had significantly higher levels of MDA (a marker of lipid peroxidation) and significantly lower TAC (a measure of antioxidant defense) compared to the healthy controls, suggesting increased oxidative stress in the hypothyroid group.

Table 4: Distribution of TNF-α Levels

Parameter	Hypothyroidism Group (n = 40)	Control Group (n = 40)	p-value
TNF-α (pg/mL)	18.2 ± 5.1	8.6 ± 2.3	<0.001

The levels of TNF-α were significantly higher in the hypothyroid group compared to the control group, indicating an inflammatory response associated with hypothyroidism.

Table 5: Correlation Coefficient of Oxidative stress marker

Parameter Pair	Correlation Coefficient (r)	P-value
MDA vs. TSH	0.78	<0.01
SOD vs. TSH	-0.62	<0.01
GPx vs. TSH	-0.55	<0.01

Table 6: Subgroup Analysis

Subgroup	MDA (Hypothyroidism vs. Control)	P-value
Age 30-40	5.9 vs. 3.3	<0.01
Age 41-50	5.7 vs. 3.1	<0.01
Age 51-55	5.5 vs. 3.0	<0.05

Table 7: Statistical Summary

Test	Application	P-value Threshold
T-test	Group comparisons	0.05
ANOVA	Subgroup analysis	0.05
Pearson Correlation	Correlation analysis	0.05

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.[12] 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. [13] 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. [14] 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 hormones causes hypothyroidism and hyperthyroidism, which leads to formation of ROS and the consequent need for antioxidants. [15]

This confirms the significance of inflammation has role in the development of thyroid dysfunctions. [16] 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. [17] In addition to inf lammatory 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. [18]

Interestingly, deiodinases are the enzy 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 nonautoimmune basis, are found to be related to OS. [19] 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. [20]

Thyroid hormones specifically T3 help to induce the HMG-CoA reductase and it is the very 1st step in the biosynthesis of cholesterol. [21] 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. [22] 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. [23] The oxidant compounds like malondialdehyde (MDA) and protein carbonyl were observed to positively correlate with anti- TPO levels, according to Nanda et al. [24]

CONCLUSION

The study of oxidative stress, thyroid profile, and TNF-α in hypothyroid patients provides valuable insights into the complex pathophysiology of the disorder. Oxidative stress and inflammation are intertwined processes that contribute to the metabolic and cardiovascular complications commonly observed in hypothyroid individuals. Further research is needed to elucidate the exact mechanisms by which these factors interact and to develop targeted therapeutic strategies to alleviate oxidative damage and inflammation in hypothyroidism. Understanding the intricate relationship between thyroid function, oxidative stress, and TNF-α is crucial for improving the clinical management of hypothyroid patients and reducing the long-term consequences of the disease

REFERENCE

1. Jakubczyk, K., et al. "Reactive Oxygen Species — Sources, Functions, Oxidative Damage." *Polski Merkuriusz Lekarski*, vol. 48, 2020, pp. 124–127.
2. Sies, Helmut, and Dean P. Jones. "Reactive Oxygen Species (ROS) as Pleiotropic Physiological Signalling Agents." *Nature Reviews Molecular Cell Biology*, vol. 21, 2020, pp. 363–383. https://doi.org/10.1038/s41580-020-0230-3.
3. Shekhova, Elena. "Mitochondrial Reactive Oxygen Species as Major Effectors of Antimicrobial Immunity." *PLoS Pathogens*, vol. 16, 2020, e1008470. https://doi.org/10.1371/journal.ppat.1008470.
4. Yang, S., and G. Lian. "ROS and Diseases: Role in Metabolism and Energy Supply." *Molecular and Cellular Biochemistry*, vol. 467, 2020, pp. 1–12. https://doi.org/10.1007/s11010-019-03667-9.
5. Di Marzo, N., E. Chisci, and R. Giovannoni. "The Role of Hydrogen Peroxide in Redox-Dependent Signaling: Homeostatic and Pathological Responses in Mammalian Cells." *Cells*, vol. 7, 2018, p. 156. https://doi.org/10.3390/cells7100156.
6. Sies, Helmut. "Hydrogen Peroxide as a Central Redox Signaling Molecule in Physiological Oxidative Stress: Oxidative Eustress." *Redox Biology*, vol. 11, 2017, pp. 613–619. https://doi.org/10.1016/j.redox.2016.12.035.
7. Sies, Helmut, Christian Berndt, and Dean P. Jones. "Oxidative Stress." *Annual Review of Biochemistry*, vol. 86, 2017, pp. 715–748. https://doi.org/10.1146/annurev-biochem-061516-045037.
8. Schieber, Michael, and Navdeep S. Chandel. "ROS Function in Redox Signaling and Oxidative Stress." *Current Biology*, vol. 24, 2014, pp. R453–R462. https://doi.org/10.1016/j.cub.2014.03.034.
9. Massart, C., et al. "Cell Biology of H_2O_2 Generation in the Thyroid: Investigation of the Control of Dual Oxidases Activity." *Molecular and Cellular Endocrinology*, vol. 343, 2011, pp. 32–44. https://doi.org/10.1016/j.mce.2011.05.047.
10. Thanas, C., P. G. Ziros, and D. V. Chartoumpekis. "The Keap1/Nrf2 Signaling Pathway in the Thyroid—2020 Update." *Antioxidants (Basel)*, vol. 9, 2020, p. 1082. https://doi.org/10.3390/antiox9111082.
11. Poncin, S., et al. "Oxidative Stress in the Thyroid Gland: From Harmlessness to Hazard Depending on the Iodine Content."

Endocrinology, vol. 149, 2008, pp. 424–433. https://doi.org/10.1210/en.2007-0951.

12. Ameziane El Hassani, R., et al. "Oxidative Stress in Thyroid Carcinomas: Biological and Clinical Significance." *Endocrine-Related Cancer*, vol. 26, 2019, pp. R131–R143. https://doi.org/10.1530/ERC-18-0476.
13. Sies, Helmut. "Oxidative Stress: A Concept in Redox Biology and Medicine." *Redox Biology*, vol. 4, 2015, pp. 180–183. https://doi.org/10.1016/j.redox.2015.01.002.
14. Filomeni, Giuseppe, et al. "Oxidative Stress and Autophagy: The Clash Between Damage and Metabolic Needs." *Cell Death & Differentiation*, vol. 22, 2015, pp. 377–388. https://doi.org/10.1038/cdd.2014.150.
15. Gu, Y., et al. "Biomarkers, Oxidative Stress and Autophagy in Skin Aging." *Ageing Research Reviews*, vol. 59, 2020, p. 101036. https://doi.org/10.1016/j.arr.2020.101036.
16. Margaritelis, Nikolaos V., et al. "Antioxidants in Personalized Nutrition and Exercise." *Advances in Nutrition*, vol. 9, 2018, pp. 813–823. https://doi.org/10.1093/advances/nmy052.
17. Guo, Q., et al. "Oxidative Stress, Nutritional Antioxidants and Beyond." *Science China Life Sciences*, vol. 63, 2020, pp. 866–874. https://doi.org/10.1007/s11427-019-9591-5.
18. Williams, N. T. "Probiotics." *American Journal of Health-System Pharmacy*, vol. 67, 2010, pp. 449–458. https://doi.org/10.2146/ajhp090168.
19. Persichetti, E., et al. "Antioxidative Capacity of *Lactobacillus fermentum* LF31 Evaluated In Vitro by Oxygen Radical Absorbance Capacity Assay." *Nutrition*, vol. 30, 2014, pp. 936–938. https://doi.org/10.1016/j.nut.2013.12.009.
20. Wang, Y., et al. "*Bacillus amyloliquefaciens* SC06 Alleviates Oxidative Stress via Modulating Nrf2/Keap1 Signaling Pathway." *Applied Microbiology and Biotechnology*, vol. 101, 2017, pp. 3015–3026. https://doi.org/10.1007/s00253-016-8032-4.
21. Knezevic, Jelena, et al. "Thyroid-Gut-Axis: How Does the Microbiota Influence Thyroid Function?" *Nutrients*, vol. 12, 2020, p. 1769. https://doi.org/10.3390/nu12061769.
22. Marrocco, I., and F. Altieri. "Measurement and Clinical Significance of Biomarkers of Oxidative Stress in Humans." *Oxidative Medicine and Cellular Longevity*, 2017, Article 6501046. https://doi.org/10.1155/2017/6501046.
23. Asra, W. A., and S. Jabeen. "Study of the Oxidative Stress, Thyroid Profile and TNF-α Among Hypothyroidism Patients." *Journal of Contemporary Clinical Practice*, vol. 10, no. 2, 2024, pp. 322–326. https://doi.org/10.18683/jccp.2018.1091/02.46