Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/5wjeyx17

# STATUS OF OXIDATIVE STRESS IN HYPOTHYROID INDIVIDUALS

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## ABSTRACT

**Introduction**- Numerous metabolic processes are regulated by thyroid hormone. A clinical condition known as hypothyroidism is characterized by decreased thyroid activity. One of the side effects of thyroid hormone abnormalities is oxidative stress. The purpose of this study was to assess the antioxidant status and oxidative stress indicators in hypothyroidism patients.

**Material and Methods**- In all, 540 participants were enrolled in the trial, including 270 patients with thyroid hormone deficiency (of which 153 had hypothyroidism) and a control group of 153 healthy patients. A venipuncture was used to draw about five milliliters (5 mL) of blood from each participant, which was then poured into a sterile, simple container. The activities of glutathione, malondialdehyde, and catalase were assessed using spectrophotometry using a UV Visible spectrophotometer.

**Result**- MDA levels, a measure of oxidative stress and lipid peroxidation, were considerably higher in the hypothyroid group ($6.86 \pm 1.76$ nmol/mL) than in the control group ($4.86 \pm 0.7$ nmol/mL), suggesting that hypothyroid people experience higher levels of oxidative stress. On the other hand, the hypothyroid group had significantly decreased antioxidant defence markers. GSH levels were also considerably lower ($60.36 \pm 7.43$ nmol/mL) than controls ($116 \pm 13.08$ nmol/mL), and catalase activity was decreased to $111 \pm 14.49$ nmol/mL in hypothyroid patients versus $163 \pm 15.99$ nmol/mL in controls.

**Conclusion**- The pathogenesis and problems linked to thyroid dysfunction may be exacerbated by hypothyroid individuals' increased oxidative stress and compromised antioxidant defences

## INTRODUCTION

As one of the main hormonal elements in the control of the basal metabolic rate of target organs, such as the liver, heart, kidneys, and brain, thyroid hormones are vital for the human body's normal physiological development [1]. Protein deterioration, oxidative metabolism, and the basal metabolic state are all modulated by thyroid hormones [2].

A hypoactive thyroid gland, which results in decreased thyroid hormone production and a variety of metabolic abnormalities, is the hallmark of hypothyroidism, a common endocrine condition [3].

The pathophysiology of hypothyroidism is increasingly influenced by oxidative stress, which is defined as an imbalance between the body's ability to detoxify free radicals through antioxidants and the creation of these radicals [4,5].

In hypothyroid patients, decreased thyroid hormone levels can worsen oxidative damage to cells and tissues by reducing the activity of antioxidant enzymes [6,7].
Patients with hypothyroidism issues had higher amounts of malondialdehyde and lipid peroxidation, as per numerous studies [8,9]. Oxidative stress, which damages proteins, DNA, and lipids, might result from an imbalance between the generation and elimination of reactive oxygen species that take place during the hypometabolic state [10].
The goal of the study was to identify oxidative stress and antioxidant status in hypothyroid patients.

## MATERIAL AND METHODS

The study was carried out at the Department of Biochemistry of Index Medical College, Indore M.P. after receiving ethical approval from the Institutional Ethics Committee.

In all, 540 participants were enrolled in the trial, including 270 patients with thyroid hormone deficiency (of which 153 had hypothyroidism) and a control group of 153 healthy patients.
Inclusion criteria- All the patients who gave their consent were included in this study.
Exclusion criteria- Individuals currently undergoing medical treatment, individuals who use tobacco or consume alcohol, pregnant and breastfeeding women, those receiving immunosuppressive therapy, as well as individuals with preexisting health conditions such as diabetes, HIV/AIDS, cardiovascular diseases, and other conditions, who did not provide their consent, were consequently excluded from the study.

### Collection of samples

For each participant, approximately five milliliters (5 mL) of blood were obtained through venipuncture and dispensed into a plain sterile container, in which it was permitted to clot. The serum was isolated via centrifugation and subsequently transferred with precision into a pre-labeled tube for the quantitative analysis of reduced glutathione, malondialdehyde, and catalase activity.
Malondialdehyde, glutathione, and catalase activities were evaluated using spectrophotometry with a UV Visible spectrophotometer, specifically the PXUV-2601 model manufactured by Panomex Inc. , located in New Delhi, India. [11-13].

### Statistical evaluation

All observations were systematically organized into tables and charts, presented as the mean ± standard deviation (SD). The statistical analysis was conducted utilizing one-way analysis of variance (ANOVA) and Student's t-test, with the assistance of the Statistical Package for Social Sciences (SPSS) version 25 (IBM, Armonk, NY, USA).

## RESULT

### Age and Gender wise distribution

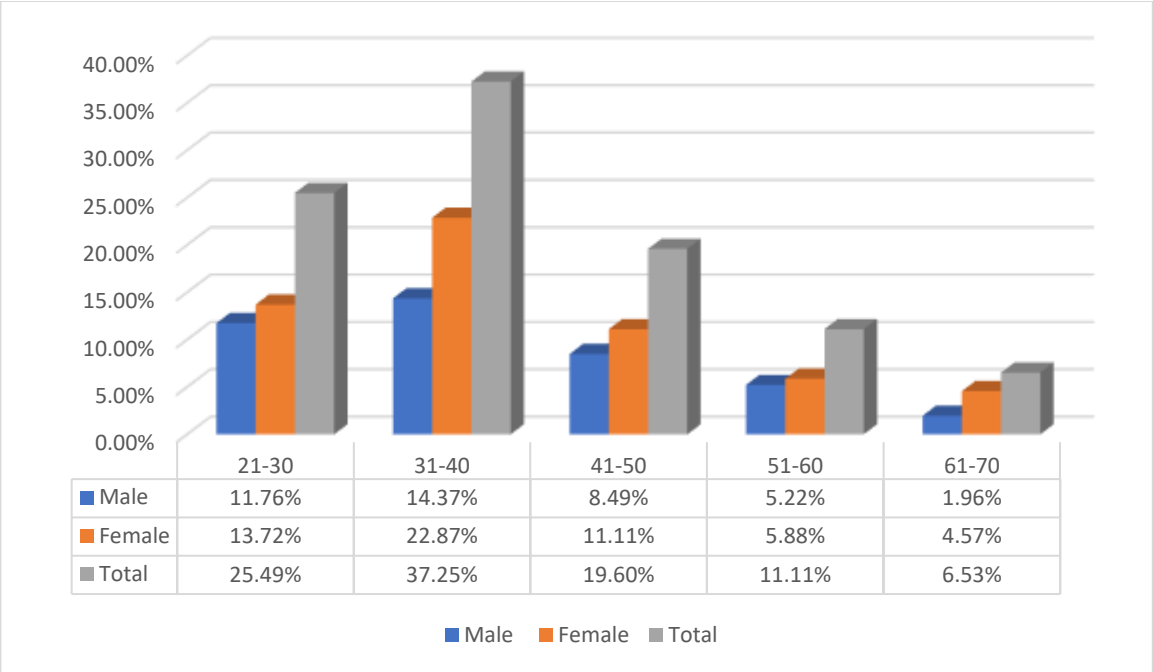
For the study, 270 people with thyroid dysfunction were recruited. The case group consisted of 270 people, 153 of whom had a diagnosis of hypothyroidism. 153 healthy controls were also included in the study.

**Age and Gender wise Distribution**

| Age | Male | Female | Total |
|---|---|---|---|
| 21-30 | 18 | 21 | 39 |
| 31-40 | 22 | 35 | 57 |
| 41-50 | 13 | 17 | 30 |
| 51-60 | 08 | 09 | 17 |
| 61-70 | 03 | 07 | 10 |

With 37.25% of the population falling within the age range of 31 to 40, the majority of participants are female (22.87%) compared to male (14.37%). The age group of 21–30, which makes up 25.49%

of the total, comes next. The age group between 41 and 50 accounts for 19.60%, while the age groups between 51 to 60 and 61 to 70 account for 11.11% and 6.53%, respectively. In general, there are more women than men in every age range, with the age group of 31 to 40 having the highest representation.

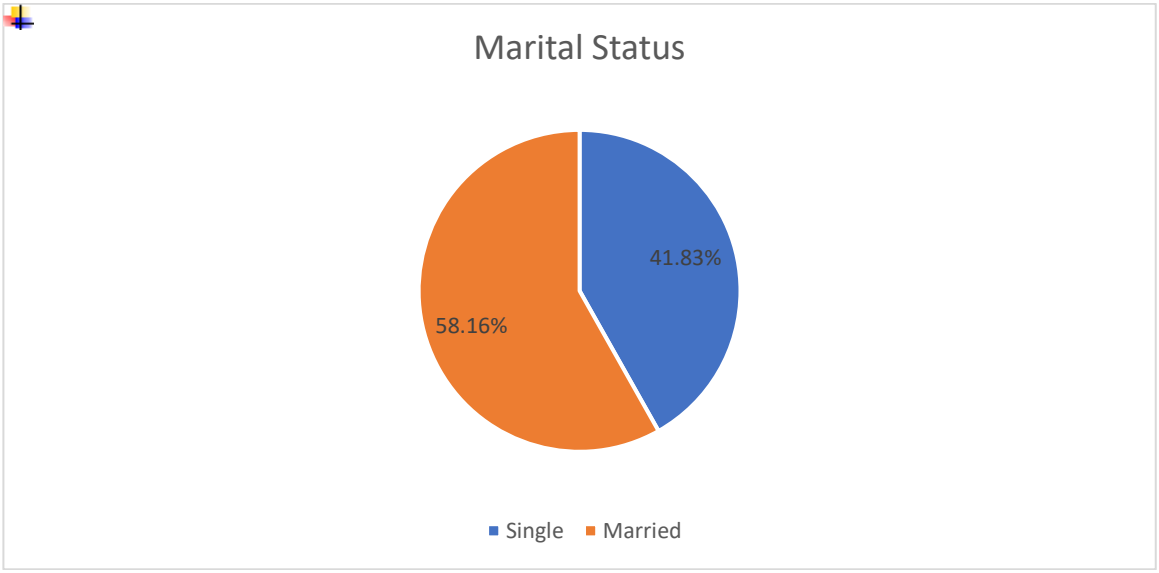



| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 |
|---|---|---|---|---|---|
| Male | 11.76% | 14.37% | 8.49% | 5.22% | 1.96% |
| Female | 13.72% | 22.87% | 11.11% | 5.88% | 4.57% |
| Total | 25.49% | 37.25% | 19.60% | 11.11% | 6.53% |

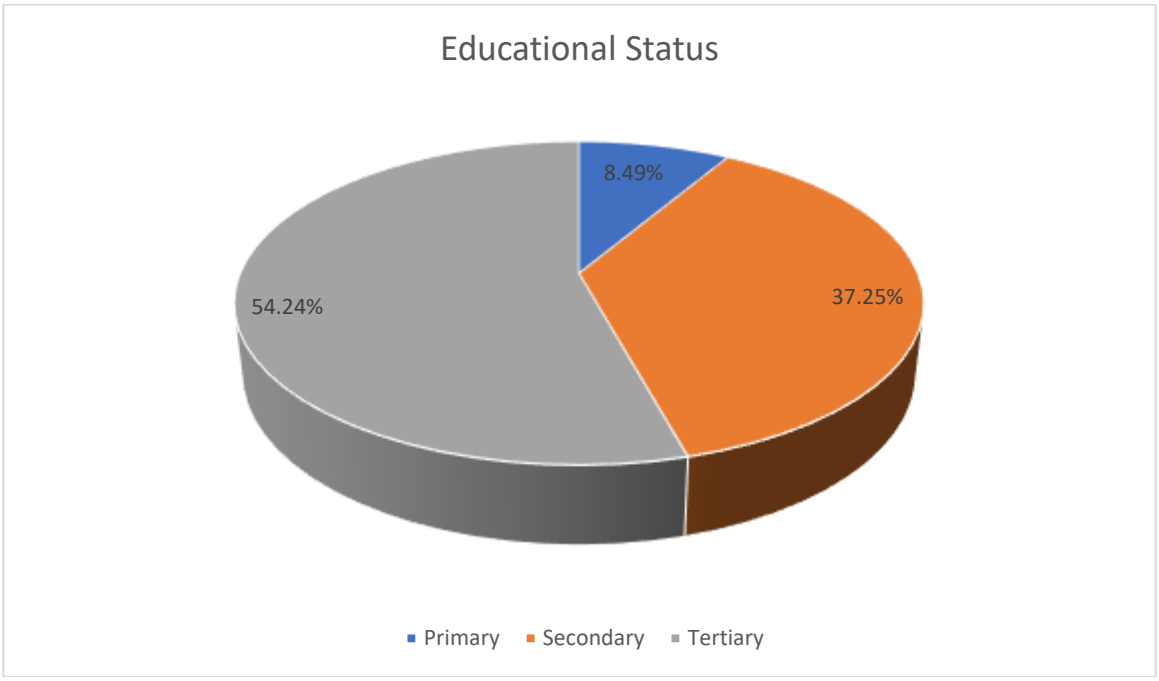
Males with hypothyroidism exhibit specific physical measuring tendencies, according to their anthropometric data. With a standard deviation of ±3.2 and an average height of 5.6 feet, the group exhibits a wide range of height variances. The standard deviation is ±5.82 and the mean weight is 82 kg, indicating that most people tend to weigh more. According to traditional BMI classifications, the group is classified as overweight because their calculated average Body Mass Index (BMI) is 25.87±2.12. This confirms the widely held clinical finding that people with hypothyroidism are more likely to acquire weight and may struggle to keep their BMI within normal limits because of slower metabolisms and other hormonal abnormalities.

There are significant differences in the anthropometric measurements of females with hypothyroidism. With a standard deviation of ±2.67 and an average height of 5.2 feet, the group shows some variation in individual stature. With a standard deviation of ±3.82 and a mean weight of 85 kg, the majority of people appear to be in the higher weight category. According to standard BMI classifications, the average Body Mass Index (BMI) is 26.56±2.97, which places the person in the overweight category. Given that decreased metabolic activity frequently results in increased body weight and a higher BMI, our findings are in line with the well-established link between hypothyroidism and weight gain.

The majority of people with hypothyroidism are married, according to data on marital status among those affected. Of the total, 64 people (41.83%) are single and 89 people (58.16%) are married. This suggests that married people are somewhat more likely than unmarried people to have hypothyroidism. This distribution may be influenced by a number of social, hormonal, or behavioral factors relating to married life.




The majority of people with hypothyroidism have a higher degree of education, according to their educational status. More than half of the group is well-educated, as evidenced by the 83 people (54.24%) who have finished tertiary education. Only 13 people (8.49%) had only primary education, whereas 57 people (37.25%) had completed secondary education. According to this distribution, hypothyroidism affects people of all educational levels, but it is more frequently seen in those with higher educational attainment. This could be because educated people are more likely to be diagnosed, have better access to healthcare, and are more conscious of their health.




**Status of pulse rate and blood pressure among study groups.**

| Variables | Hypothyroid | Control | p value |
|---|---|---|---|
| Pulse in bpm | 116±4.72 | 88±4.98 | <0.001 |
| Systolic BP | 133±8.98 | 129±4.71 | <0.001 |
| Diastolic BP | 100±7.65 | 87±6.12 | <0.001 |

There are statistically significant variations in the vital signs of hypothyroid people compared to the control group. With a p-value of <0.001, the hypothyroid group's average pulse rate is significantly

higher at 116±4.72 beats per minute (bpm) than the control group's, which is 88±4.98 bpm. This difference is statistically significant. Likewise, the hypothyroid group's systolic blood pressure (133±8.98 mmHg) is marginally higher than that of the control group (129±4.71 mmHg), with a p-value of less than 0.001. The hypothyroid group's average diastolic blood pressure is 100±7.65 mmHg, while the control group's is 87±6.12 mmHg. This difference is more noticeable.
These results imply that hypothyroidism is linked to raised blood pressure and pulse rate, which could be caused by underlying hormonal abnormalities that impact cardiovascular function. The reliability of these observed differences is further supported by the statistically significant p-values for each variable.

**Gender-wise distribution of antioxidant and oxidative stress**

| Parameter (nmol/mL) | Male | Female |
|---|---|---|
| MDA | 4.52± 1.2 | 4.02± 0.98 |
| Catalase | 226.97± 35.03 | 179± 33.83 |
| GSH | 77.58± 17.65 | 84.36± 14.78 |

Males had slightly higher MDA levels (4.52 ± 1.2 nmol/mL) than females (4.02 ± 0.98 nmol/mL), which suggests that males are under more oxidative stress. MDA levels are a measure of lipid peroxidation and oxidative stress. Males had higher levels of catalase activity (226.97 ± 35.03 nmol/mL) than females (179 ± 33.83 nmol/mL), a crucial antioxidant enzyme that aids in the breakdown of hydrogen peroxide. This suggests that males had a better enzymatic antioxidant response. However, females had greater levels of GSH (84.36 ± 14.78 nmol/mL) than males (77.58 ± 17.65 nmol/mL), indicating superior non-enzymatic antioxidant defense. GSH is a non-enzymatic antioxidant that shields cells from harm caused by free radicals.
Overall, the evidence points to gender-based variations in antioxidant defence systems and oxidative stress, with females having comparatively higher glutathione levels and males exhibiting higher levels of catalase and oxidative stress.

**Comparative Distribution of antioxidant and oxidative stress status of subjects**

| Parameter (nmol/mL) | Hypothyroid | Control |
|---|---|---|
| MDA | 6.86± 1.76 | 4.86± 0.7 |
| Catalase | 111± 14.49 | 163± 15.99 |
| GSH | 60.36± 7.43 | 116± 13.08 |

MDA levels, a measure of oxidative stress and lipid peroxidation, were considerably higher in the hypothyroid group (6.86 ± 1.76 nmol/mL) than in the control group (4.86 ± 0.7 nmol/mL), suggesting that hypothyroid people experience higher levels of oxidative stress. On the other hand, the hypothyroid group had significantly decreased antioxidant defense markers. GSH levels were also considerably lower (60.36 ± 7.43 nmol/mL) than controls (116 ± 13.08 nmol/mL), and catalase activity was decreased to 111 ± 14.49 nmol/mL in hypothyroid patients versus 163 ± 15.99 nmol/mL in controls. The pathogenesis and problems linked to thyroid dysfunction may be exacerbated by hypothyroid individuals' increased oxidative stress and compromised antioxidant defenses.

**Discussion**

A serum TSH concentration that is higher than the statistically determined upper limit of the reference range is referred to be hypothyroidism. The pathological effects of hypothyroidism suggest that an antioxidant imbalance may be quite likely. In line with Kale [14] Oxidative metabolism is increased and cellular processes are accelerated by thyroid hormones. Heat is generated as ATP generation rises due to the stimulation of enzymes that regulate active transport pumps, which raises the demand for cellular oxygen. Oxidative stress may result from immunosuppression brought on by hypothyroidism.

Higher concentrations of TSH may cause the release of inflammatory cytokines and lower antioxidant state, according to Yilmaz A et al. [15], while Carmeli E., Bachar, A et al. [16] reported Oxidative stress linked to hypothyroidism results from both a decrease in the anti-oxidative defense system's ability and an increase in free radical generation. Because of their established effects on mitochondrial respiration, changes in thyroid hormone levels may be one of the primary physiological modulators of in vivo cellular oxidative stress.

Specifically, it has been proposed that a lipid peroxidative response may result from an oxidative stress situation in the liver, heart, and certain skeletal muscles brought on by an increase in reactive oxygen species brought on by a thyroid hormone shortage [17]. Oxidative stress can also be exacerbated by metabolic disorders resulting from autoimmune-based hypothyroidism.

According to the results of the current study, 15.3% of the older urban cohort from M.P. had hypothyroidism. Overt hypothyroidism was shown to be 10.95% prevalent in a previous study by Unnikrishnan et al. [18]. The prevalence in our study was higher in females than in males, which is consistent with the findings of Mirahmad M et al. et al. [19]

According to Gussekloo, J. et al. [20], the study found that people with hypothyroidism had significantly higher levels of several lipid parameters. It also showed that women are more likely than men to have hypothyroidism, and that men who have it have a higher mortality rate in a middle-aged group. It is crucial to recognize that cognitive impairments are not unique to women with hypothyroidism. According to a previous study by Eslami-Amirabadi and associates, [21], most women with hypothyroidism have deficits in at least one cognitive domain, with attention being consistently noted as a domain that is impacted.

Patients who had been diagnosed with hypothyroidism before therapy began had higher levels of malondialdehyde (MDA) than the control group. Previous studies have indicated a decrease in malondialdehyde (MDA) levels in hypothyroidism patients after treatment. [22–24] The results of our study were also similar.

According to the current study, the hypothyroid group had the greatest concentration of malondialdehyde (MDA), a biomarker of lipid peroxidation, at 6.86 ± 1.76 nmol/mL. The hypothyroid group exhibits the lowest enzymatic activity of catalase, which neutralizes hydrogen peroxide, with a reading of 111 ± 14. 49 nmol/mL. Following treatment with antioxidants alone, Guerra and colleagues [25] found that individuals with hyperthyroidism had lower MDA levels and increased antioxidant enzyme activity. Following therapy with a combination of antithyroid drugs and antioxidants, the study also found that individuals with hyperthyroidism had rapid improvements in malondialdehyde (MDA) levels and antioxidant enzyme activity. Claudio and colleagues [26] also noted that taking antioxidant supplements along with the antithyroid drug had a beneficial impact.

## CONCLUSION

Since OS in hypothyroidism is a complex disorder, it may be the cause of the comorbidities linked to this illness if it is not given the attention it needs. Further cohorts and clinical trials involving antioxidant supplementation in addition to conventional treatment should be conducted for hypothyroid patients, given the numerous studies that have reported OS in hypothyroidism, as well as the existence of cardiovascular risk factors and an atherogenic biochemical profile.

## Reference

1.Guerrero, A., Pamplona, R., Postero-Otin, M., et al., 1999. Effect of thyroid status on lipid composition and peroxidation in the mouse liver. Free Radic. Biol. Med. 26 (1-2), 73–80.
2.Katzung et al. “Basic and Clinical Pharmacology”, 13th edition.
3.Wouters HJ, Slagter SN, Muller Kobold AC, van der Klauw MM, Wolffenbuttel BH. Epidemiology of thyroid disorders in the Lifelines Cohort Study (the Netherlands). PLoS One. 2020 Nov 25;15(11).

4.Elnakish MT, Ahmed AA, Mohler PJ, Janssen PM. Role of oxidative stress in thyroid hormone-induced cardiomyocyte hypertrophy and associated cardiac dysfunction: an undisclosed story. Oxidative Medicine and Cellular Longevity. 2015 Oct;2015. **10.1155/2015/854265**
5. Rasool M, Malik A, Saleem S, Ashraf MA, Khan AQ, Waquar S, Zahid A, Shaheen S, Abu-Elmagd M, Gauthaman K, Pushparaj PN. Role of oxidative stress and the identification of biomarkers associated with thyroid dysfunction in schizophrenics. Frontiers in pharmacology. 2021 Apr 29;12:646287. 10.3389/fphar.2021.646287
6. Corssac GB, de Castro AL, Tavares AV, Campos C, Fernandes RO, Ortiz VD, Siqueira R, Fernandes TR, Belló-Klein A, Araujo AS. Thyroid hormones effects on oxidative stress and cardiac remodeling in the right ventricle of infarcted rats. Life sciences. 2016 Feb 1;146:109-16.10.1016/j.lfs.2015.12.052
7. Wouters HJ, Slagter SN, Muller Kobold AC, van der Klauw MM, Wolffenbuttel BH. Epidemiology of thyroid disorders in the Lifelines Cohort Study (the Netherlands). PLoS One. 2020 Nov 25;15(11):e0242795. 10.1371/journal.pone.0242795
8. Panda S, Dash MK, Thatoi PK, Dandapat J. Rath B. Oxidative stress correlates well with markers of metabolic syndrome in clinically hypothyroid cases: a hospital-based case-control study in a remote tribal district. *RUDN J Med.* 2021;25(1):55- 65. doi: 10.22363 /2313-0245-2021-25-1-55-65
9. Torun AN, Kulaksizoglu S, Kulaksizoglu M, et al. Serum total antioxidant status and lipid peroxidation marker malondialdehyde levels in overt and subclinical hypothyroidism. *Clin Endocrinol*. 2009;70(3): 469-474.
10. Santi A, Duarte MM, deMenezes CC, Loro VL. Association of Lipids with Oxidative Stress Biomarkers in Subclinical Hypothyroidism. *Int J Endocrinol*. 2012:856359. doi: 10.1155/2012/856359
11.Nandi A, Yan LJ, Jana CK, Das N. Role of Catalase in Oxidative Stress- and Age-Associated Degenerative Diseases. *Oxid Med Cell Longev.* 2019;19:9613090. doi: 10.1155/2019/9613090.
12.Lu SC, Kwon IP, Pei CO, Chen CZ. Glutathione synthesis. *Biochim Biophys Acta*. 2013;30(5):3143-3153. doi: 10.1016/j.bbagen.2012.09.008.
13.Gaucher C, Boudier A, Bonetti J, Clarot I, Leroy P, Parent M. Glutathione: Antioxidant Properties Dedicated to Nanotechnologies. *Antioxidant.* 2018;7(5):62-64. doi: 10.3390/antiox7050062.
14. Kale M, Umathe SN, Bhusari KP. Oxidative stress and the thyroid. Positive Health 2006 ecognitive.com; 21-27.
15. Yilmaz S, Ozan S, Benzer F, Canatan H. Oxidative damage and antioxidant enzyme activities in experimental hypothyroidism. Cell Biochem Funct 2003; 21 (4): 325-330.
16. 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. Res. Development. Disab. 2008, 29: 431-438.
17. Nanda N, Bobby Z, Hamide A. Association of thyroid stimulating hormone and coronary lipid risk factors with lipid peroxidation in hypothyroidism; Clinical Chem Lab Med, 2008; 46 (5): 674-679.
18. Unnikrishnan A, Kalra S, Sahay R, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian J Endocrinol Metab*. 2013;17(4):647.
19. Mirahmad M, Mansour A, Moodi M, *et al.* Prevalence of thyroid dysfunction among Iranian older adults: A cross-sectional study. *Sci Rep*. 2023;13(1):21651.
20. Gussekloo J, Van Exel E, De Craen AJM, Meinders AE, Frölich M, Westendorp RGJ. Thyroid status, disability and cognitive function, and survival in old age. *JAMA*. 2004;292(21):2591-2599.
21. Eslami-Amirabadi M, Sajjadi SA. The relation between thyroid dysregulation and impaired cognition/behaviour: An integrative review. *J Neuroendocrinol*. 2021;33(3):e12948

22. Erdamar H, Demirci H, Yaman H, Erbil MK, Yakar T, Sancak B, *et al.* The effect of hypothyroidism, hyperthyroidism, and their treatment on parameters of oxidative stress and antioxidant status. Clin Chem Lab Med 2008;46:1004-10.
23. Drutel A, Archambeaud F, Caron P. Selenium and the thyroid gland: More good news for clinicians. Clin Endocrinol (Oxf) 2013;78:155-64.
24. Bhimte B, Agrawal BK, Sharma VK, Chauhan SS. Oxidative stress status in hypothyroid patients. Biomed Res 2012;23:286-8.
25. Guerra, L.N., Rios de Molina, M., del, C., Miler, E.A., Moiguer, S., Karner, M., Burdman, J.A., 2005. Antioxidants and methimazole in the treatment of Grave's disease: effect on urinary malondialdehyde levels. Clin. Chim. Acta 352, 115–120.
26. Claudio, Marcocci, Marenza, L., Maria, A.A., 2012. Oxidative stress in graves' disease. Eur. Thyroid J. 1, 80–87.