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Original Research Article

Evaluation of Oxidative Stress, Antioxidant Markers, and Thyroid Stimulating Hormones in Hyperthyroid Disorders: A Case-Control Study in Central India

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Abstract

Background: Hyperthyroidism, a prevalent endocrine disorder, leads to increased production of thyroid hormones such as T3 and T4. This elevation accelerates basal metabolic processes and mitochondrial respiration, resulting in excessive generation of reactive oxygen species (ROS). When these ROS overwhelm the body's antioxidant defenses, oxidative stress ensues, damaging lipids, proteins, and DNA.

Objective: To assess oxidative stress levels, antioxidant markers, and thyroid stimulating hormone (TSH) levels in patients with hyperthyroidism and compare them to healthy controls.

Methods: This case-control study was conducted at Index Medical College Hospital & Research Centre, Indore, and Madhya Pradesh. A total of 69 hyperthyroid patients and 204 healthy controls were recruited. Biochemical parameters including serum T3, T4, TSH, malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant capacity (TAC), Vitamin C, and Vitamin E were measured using validated protocols. Statistical analysis was performed using Student's t-test and p-values <0.05 were considered significant.

Results: MDA levels were significantly elevated in hyperthyroid patients (7.8 ± 1.1 nmol/L) compared to controls (1.07 ± 0.61 nmol/L, $p<0.0001$), indicating increased lipid peroxidation. TAC, Vitamin C, and Vitamin E levels were significantly lower in hyperthyroid cases ($p<0.0001$), suggesting depleted antioxidant reserves. T3 and T4 levels were markedly increased, while TSH levels were significantly suppressed in hyperthyroid patients compared to controls.

Conclusion: The study confirms a strong association between hyperthyroidism and oxidative stress, with marked alterations in antioxidant profiles. Monitoring these parameters could be beneficial in understanding disease progression and guiding supportive antioxidant therapy in clinical practice.

Keywords: Hyperthyroidism, Oxidative Stress, Antioxidants, Thyroid Stimulating Hormone (TSH), MDA, SOD, TAC, Vitamin C, Vitamin E.

Introduction

Thyroid hormones-triiodothyronine (T3) and thyroxine (T4)-play an essential role in regulating metabolism, thermogenesis, and cellular function. Hyperthyroidism, a condition marked by the overproduction of these hormones, results in enhanced basal metabolic rate and increased mitochondrial activity. This hypermetabolic state leads to the excessive production of reactive oxygen species (ROS), creating an imbalance between oxidants and antioxidants, a condition known as oxidative stress [1]. Oxidative stress is implicated in a wide array of pathological processes, including DNA damage, lipid peroxidation, and protein modification. The body's defense against oxidative stress comprises enzymatic antioxidants like superoxide dismutase

(SOD) and non-enzymatic molecules such as Vitamin C, Vitamin E, and total antioxidant capacity (TAC). When antioxidant systems are overwhelmed by ROS, cellular injury and systemic inflammation may result [2]. Recent studies have revealed a bidirectional relationship [3] between thyroid dysfunction and oxidative stress. Hyperthyroidism has been associated with increased lipid peroxidation, reduced antioxidant enzyme activity, and compromised total antioxidant levels. These changes can contribute to clinical manifestations [4] of hyperthyroidism such as fatigue, cardiovascular strain, muscle wasting, and impaired neurocognitive function.

India is witnessing a rise in thyroid disorders, particularly in iodine-sufficient regions like Central India. However, limited data exists on the biochemical interplay between oxidative stress and hyperthyroidism in this region. Given the potential role of oxidative imbalance [5] in disease progression, evaluating oxidative stress markers and antioxidants in hyperthyroid patients can offer valuable insights for diagnosis, prognosis, and therapeutic management. The present study aims to evaluate and compare the levels of oxidative stress markers (malondialdehyde - MDA)[6], enzymatic antioxidants (SOD), non-enzymatic antioxidants (Vitamin C and E), and total antioxidant capacity (TAC), alongside thyroid function parameters (TSH, T3, T4)[7], between hyperthyroid patients and healthy controls in a Central Indian population[8].

Materials and Methods

Study Design and Setting: This was a hospital-based case-control study conducted at the Department of Biochemistry, Index Medical College Hospital & Research Centre (IMCHRC), Indore, and Madhya Pradesh. Ethical clearance was obtained from the Institutional Ethical Committee prior to commencement.

Study Population

Cases (Hyperthyroid Group): A total of 69 patients clinically diagnosed with hyperthyroidism were recruited from the OPD of Medicine and Endocrinology. Hyperthyroidism was confirmed by elevated T3 and T4 levels with suppressed TSH.

Controls: 204 age- and gender-matched healthy individuals with normal thyroid function tests were included as the control group.

Inclusion Criteria

- Age between 20-70 years
- Newly diagnosed and untreated hyperthyroid patients (for the case group)
- Apparently healthy individuals with normal thyroid function (for the control group)

Exclusion Criteria

Subjects with the following conditions were excluded:

- Diabetes mellitus
- Hypertension
- Renal or hepatic dysfunction
- Inflammatory or autoimmune diseases
- Pregnancy or post-menopausal status
- Alcohol or tobacco use
- Vitamin supplementation or antioxidant therapy within the past 3 months

Sample Size Calculation

The sample size for the study was calculated using the formula:

$$n = \frac{4pq}{e2}$$

Where:

- p = prevalence of thyroid dysfunction = 15%
- q = 100 -p
- e = margin of error = 5%

Using this, a total sample size of 204 participants was determined, with 69 hyperthyroid cases identified among them.

Sample Collection and Processing

- 5 mL of venous blood was collected from each participant under aseptic conditions.
- Blood was centrifuged at 3000 rpm for 10 minutes to separate serum.
- All biochemical estimations were carried out within 4 hours of sample collection.

Table 1: Biochemical Parameters Assessed

Parameter	Method Used
T3, T4, TSH	Finecare™ FIA Meter - Immunofluorescence Assay
Malondialdehyde (MDA)	Kei Satoh TBARS Method
Superoxide Dismutase (SOD)	Kono A. Method (NBT Reduction)
Total Antioxidant Capacity (TAC)	FRAP (Ferric Reducing Ability of Plasma)
Vitamin C	DNPH Colorimetric Method (Rosenberg)
Vitamin E	Dipyridyl Ferric Chloride Method (Rosenberg)

Statistical Analysis

- Data were expressed as Mean ± Standard Deviation (SD).
- Comparisons between hyperthyroid and control groups were made using independent Student's t-test.
- A p-value of <0.05 was considered statistically significant.
- All statistical analyses were performed using SPSS v20.0 software.

Results

A total of 69 hyperthyroid patients and 204 healthy controls were evaluated for thyroid function, oxidative stress, and antioxidant status. The findings are presented in the form of tables and figures based on your original thesis data.

Table 2: Thyroid Function Parameters

Parameter	Hyperthyroid (Mean ± SD)	Control (Mean ± SD)	p-value
T3 (ng/mL)	5.34 ± 3.12	1.17 ± 0.38	<0.0001
T4 (µg/dL)	19.21 ± 5.54	7.31 ± 2.21	<0.0001
TSH (µIU/mL)	0.12 ± 0.08	2.87 ± 1.11	<0.0001

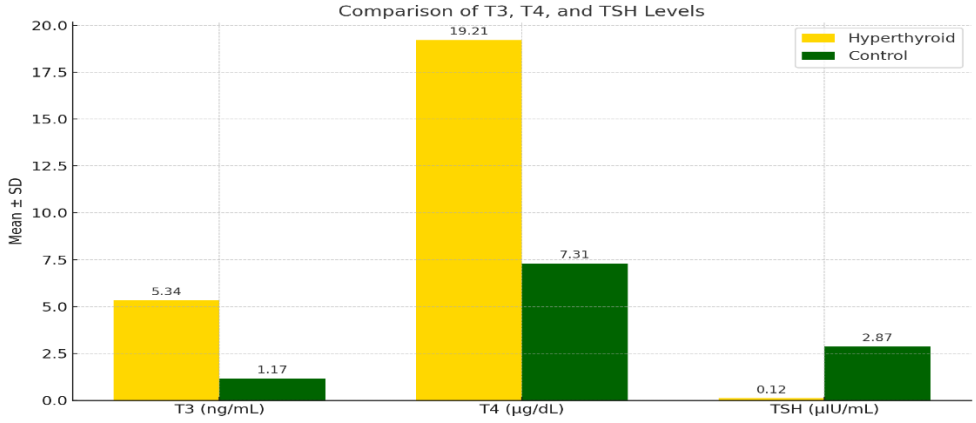

Figure 1: Comparison of T3, T4, and TSH between hyperthyroid and control groups

The graph shows that hyperthyroid patients have significantly higher T3 and T4 levels and markedly lower TSH levels compared to controls ($p < 0.0001$), reflecting the typical hormonal imbalance seen in hyperthyroidism.

Table 3: Oxidative Stress and Antioxidant Markers

Marker	Hyperthyroid	Control	p-value
MDA (nmol/L)	7.8 ± 1.1	1.07 ± 0.61	<0.0001
SOD (U/mL)	3.22 ± 1.12	3.42 ± 0.95	0.150
TAC (mmol/L)	0.89 ± 0.12	1.84 ± 0.21	<0.0001
Vitamin C (mg/dL)	0.80 ± 0.14	1.21 ± 0.11	<0.0001
Vitamin E (µg/dL)	0.60 ± 0.08	6.86 ± 1.03	<0.0001

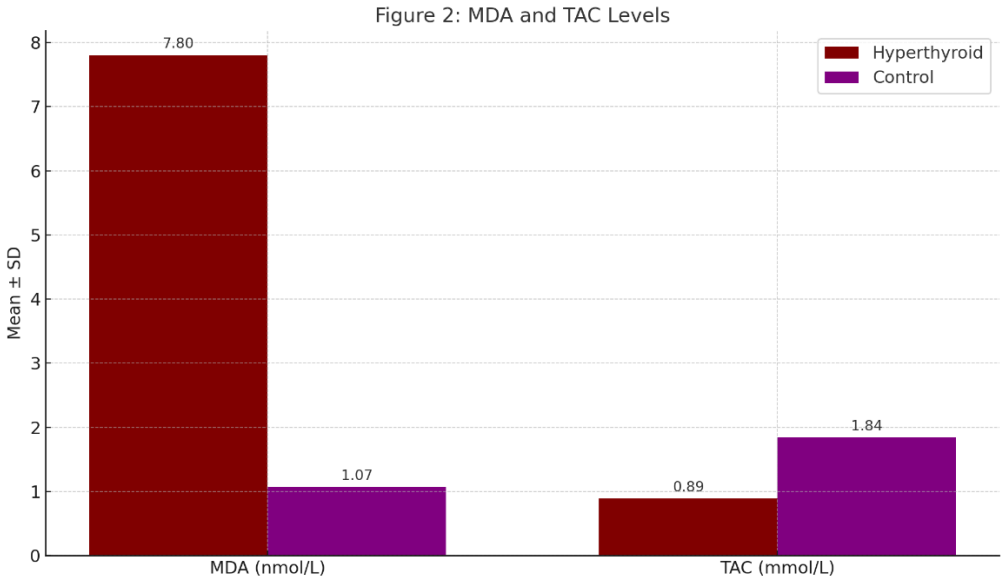

Figure 2: Elevated MDA and decreased TAC levels in hyperthyroid group

MDA levels are elevated, and TAC levels are decreased in hyperthyroid subjects, indicating increased oxidative stress and reduced antioxidant defense.

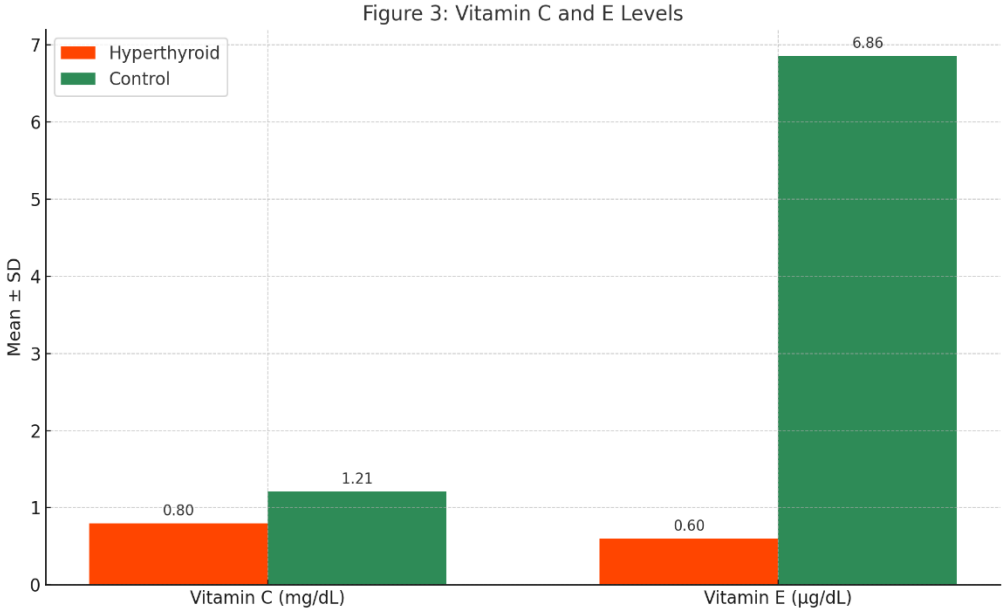

Figure 3: Reduced Vitamin C and Vitamin E in hyperthyroid subjects

This reduction highlights a compromised antioxidant defense mechanism, contributing to oxidative stress in hyperthyroid conditions.

- MDA levels were significantly increased in hyperthyroid patients, indicating enhanced lipid peroxidation and oxidative damage.
- TAC, Vitamin C, and Vitamin E levels were significantly lower in the hyperthyroid group, pointing to antioxidant depletion.
- SOD levels showed a non-significant decline, suggesting possible compensatory upregulation.

Table 4:Additional Biochemical Parameters

Parameter	Hyperthyroid	Control	p-value
Uric Acid (mg/dL)	5.97 ± 0.73	4.57 ± 0.62	<0.0001
Total Bilirubin (mg/dL)	1.28 ± 0.21	0.93 ± 0.12	<0.0001
Serum Albumin (g/dL)	3.85 ± 1.15	4.23 ± 1.24	0.0259

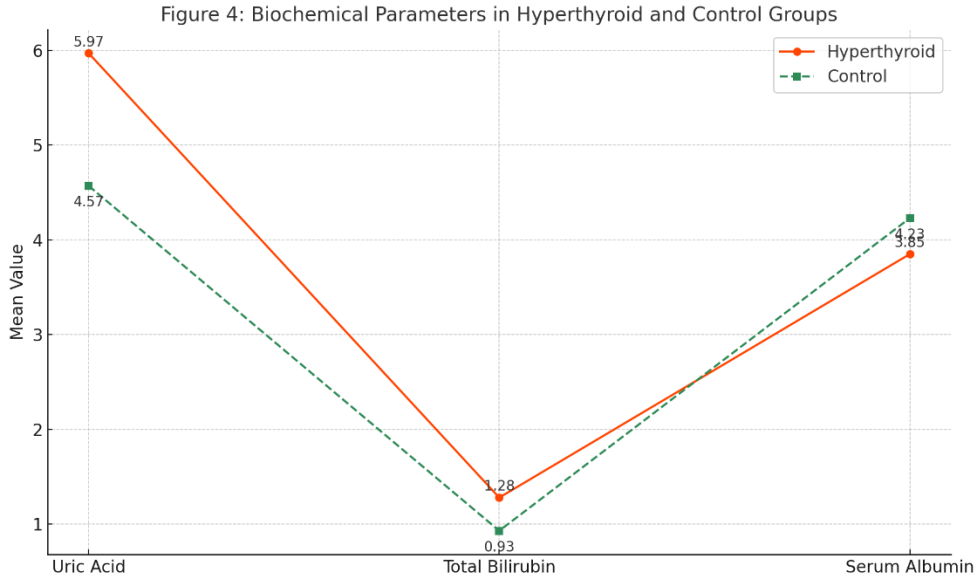

Figure 4: Elevated uric acid and bilirubin levels; reduced albumin in hyperthyroid subjects

- Elevated uric acid and bilirubin levels suggest altered purine metabolism and hepatic oxidative stress.
- Lower albumin, a transport protein with antioxidant properties, reflects systemic inflammation and protein loss.

Summary of Key Findings:

- Hyperthyroid patients exhibited significantly higher oxidative stress (↑ MDA).
- Antioxidant markers were significantly reduced (↓ TAC, Vitamin C, Vitamin E).
- Thyroid hormones showed the expected profile**:** ↑ T3/T4, ↓ TSH.
- Biochemical abnormalities such as ↑ uric acid and ↓ albumin add clinical insight into systemic effects.

Discussion

This study highlights a significant correlation between hyperthyroidism and oxidative stress, emphasizing the biochemical and clinical importance of redox imbalance in thyroid dysfunction.

A. Oxidative Stress in Hyperthyroidism: Hyperthyroidism elevates T3 and T4 levels, increasing mitochondrial activity and ATP production, which leads to excess reactive oxygen species (ROS) and resulting oxidative stress that damages lipids, proteins, and DNA. [9].

In our study, MDA levels were markedly higher in hyperthyroid patients (7.8 ± 1.1 vs. 1.07 ± 0.61 nmol/L), indicating increased lipid peroxidation and supporting prior evidence of oxidative membrane damage in hyperthyroidism. [6].

B. Antioxidant Depletion in Hyperthyroidism: Total Antioxidant Capacity (TAC) was significantly reduced in hyperthyroid patients, indicating rapid depletion of antioxidant reserves against excessive ROS. Vitamin C and E levels were also markedly lowered ($p<0.0001$), reflecting diminished non-enzymatic defense against oxidative damage. [2, 10]. Their decline in serum is indicative of active antioxidant utilization in response to oxidative stress.

SOD levels were slightly lower in hyperthyroid patients (3.22 ± 1.12 vs. 3.42 ± 0.95 U/mL), though not statistically significant, possibly reflecting early compensatory antioxidant response that diminishes with disease progression [9].

C. Alterations in Biochemical Markers: Elevated uric acid in hyperthyroidism may indicate altered purine metabolism or a compensatory antioxidant response, while increased bilirubin could result from hepatic oxidative stress or hemolysis [11]. Reduced serum albumin may reflect impaired hepatic synthesis or inflammation; its antioxidant role means deficiency may worsen oxidative stress.[12].

D. Clinical and Pathophysiological Implications: This study highlights that hyperthyroidism involves not just hormone excess but significant oxidative imbalance, potentially driving symptoms like fatigue, weight loss, and cardiovascular or neuromuscular complications. Assessing oxidative stress and antioxidant levels can aid hyperthyroid management, and adjunctive supplementation (e.g., Vitamins C, E, selenium, zinc) may enhance therapeutic outcomes [13].

E. Comparison with Previous Literature

Our findings align with those of Ates and Mancini et al., confirming oxidative stress and antioxidant depletion in hyperthyroidism, with added relevance due to limited Indian data.

Limitations

- The study is limited by its single-center design.
- Only serum biomarkers were assessed; tissue-level oxidative changes were not evaluated.
- The sample size of hyperthyroid cases, though statistically adequate, could be expanded in future multicenter studies.

Conclusion

This study provides strong evidence that hyperthyroidism is significantly associated with oxidative stress, as reflected by elevated malondialdehyde (MDA) levels and diminished antioxidant reserves including total antioxidant capacity (TAC), Vitamin C, and Vitamin E. Although superoxide dismutase (SOD) did not significantly differ from controls, the cumulative decline in antioxidant defense suggests a net oxidative imbalance. The altered biochemical parameters, including raised uric acid and bilirubin levels and reduced albumin, further substantiate the systemic metabolic impact of hyperthyroid states.

These findings underline the importance of monitoring redox biomarkers in hyperthyroid patients-not only for diagnostic and prognostic purposes, but also to explore adjunct antioxidant therapies as a part of comprehensive management.

Future research should focus on longitudinal intervention studies, especially in Indian populations, to evaluate the therapeutic potential of antioxidant supplementation alongside anti-thyroid pharmacotherapy.

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