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Original Research Article

Oxidative Stress, Thyroid Stimulating Hormones, and Antioxidants in Hypothyroid Disorders: A Case-Control Study in Central India

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Conflict of interest: Nil

Abstract:

Background: Hypothyroidism is a common endocrine disorder characterized by decreased secretion of thyroid hormones, leading to a reduced metabolic rate. Emerging evidence suggests that thyroid dysfunction may be linked with oxidative stress due to impaired balance between reactive oxygen species (ROS) and antioxidant defense mechanisms.

Objective: To evaluate the levels of oxidative stress markers and antioxidant status in patients with hypothyroidism, and to examine the association between these parameters and thyroid-stimulating hormone (TSH) levels in a Central Indian population.

Methods: This case-control study was conducted at Index Medical College Hospital & Research Centre, Indore. A total of 135 hypothyroid patients and 204 age- and gender-matched healthy controls were included. Serum levels of malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant capacity (TAC), Vitamin C, Vitamin E, T3, T4, and TSH were measured using standardized spectrophotometric and immunoassay techniques. Statistical significance was assessed using t-tests and Pearson's correlation analysis.

Results: Hypothyroid patients showed significantly elevated MDA levels (3.1 ± 0.9 nmol/L vs. 1.07 ± 0.61 in controls, $p < 0.0001$), and reduced SOD (2.80 ± 0.11 U/mL), TAC (0.72 ± 0.31 mmol/L), Vitamin C (0.91 ± 0.12 mg/dL), and Vitamin E (0.66 ± 0.07 µg/dL) compared to controls ($p < 0.0001$ for all). TSH was significantly elevated. Pearson correlation showed MDA positively correlated with hypothyroidism ($r = 0.45$, $p < 0.001$), while SOD had a weak negative correlation ($r = -0.31$, $p = 0.015$) and TAC had a moderate positive correlation ($r = 0.55$, $p < 0.001$).

Conclusion: Hypothyroidism is associated with increased oxidative stress and significantly impaired antioxidant defenses. These findings suggest a potential role for antioxidant monitoring and supplementation as adjunct therapy in the management of hypothyroid disorders.

Keywords: Hypothyroidism, Oxidative Stress, Antioxidants, Malondialdehyde, SOD, TAC, Vitamin C, Vitamin E, TSH.

Introduction

Hypothyroidism is a common endocrine disorder marked by reduced secretion of thyroid hormones (T3 and T4)[1], leading to a slowed metabolism and systemic dysfunction. In recent years, its association with oxidative stress-an imbalance between reactive oxygen species (ROS) and antioxidant defenses-has gained clinical relevance.

ROS can damage cellular lipids, proteins, and DNA. The body counters this with antioxidants like superoxide dismutase (SOD), Vitamin C, Vitamin E, and total antioxidant capacity (TAC). In hypothyroidism, metabolic slowdown and mitochondrial dysfunction may impair antioxidant activity, increasing oxidative damage [2].

Studies have shown elevated malondialdehyde (MDA) and reduced antioxidant markers in hypothyroid patients [3, 4], but data from Central India remain scarce.

This study evaluates oxidative stress markers (MDA), antioxidants (SOD, Vitamin C, Vitamin E, TAC), and thyroid hormones (TSH, T3, T4) in hypothyroid patients versus healthy controls, and explores their correlation with TSH levels.

Materials and Methods

Study Design and Setting: A hospital-based case-control study was conducted in the Department of Biochemistry at Index Medical College Hospital & Research Centre, Indore, and Madhya Pradesh. Ethical clearance was obtained from the institutional ethics committee prior to initiating the study.

Study Participants

Cases (Hypothyroid Group): 135 patients with newly diagnosed primary hypothyroidism**,** confirmed by elevated TSH and reduced T3/T4 levels.

Controls: 204 age- and gender-matched thyroid individuals with no history of thyroid dysfunction.

Inclusion Criteria: Participants aged 20 to 70 years were included in the study. The case group comprised individuals with biochemically confirmed hypothyroidism, while the control group consisted of healthy individuals with a normal thyroid profile.

Exclusion Criteria: Individuals were excluded if they had diabetes, cardiovascular, renal, or liver disorders, were pregnant or postmenopausal, had a history of vitamin or antioxidant use, or were smokers, alcohol users, or had other chronic illnesses.

Sample Collection and Processing

- 5 mL of venous blood was collected under aseptic conditions.
- Blood was centrifuged to obtain serum, which was used for biochemical analysis within 4 hours of collection.

Table 1: Biochemical Parameters Measured

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

Statistical Analysis

- Data were expressed as Mean ± SD.
- Group comparisons were done using independent Student's t-test.
- Pearson's correlation was applied to examine associations between TSH and oxidative parameters.
- A p-value of<0.05 was considered statistically significant.
- All analyses were performed using SPSS v20.0software.

Results: Thyroid Profile: Patients with hypothyroidism (n = 135) exhibited a significant alteration in thyroid hormones compared to controls (n = 204). Specifically:

- TSH was elevated
- T3 and T4 levels were reduced

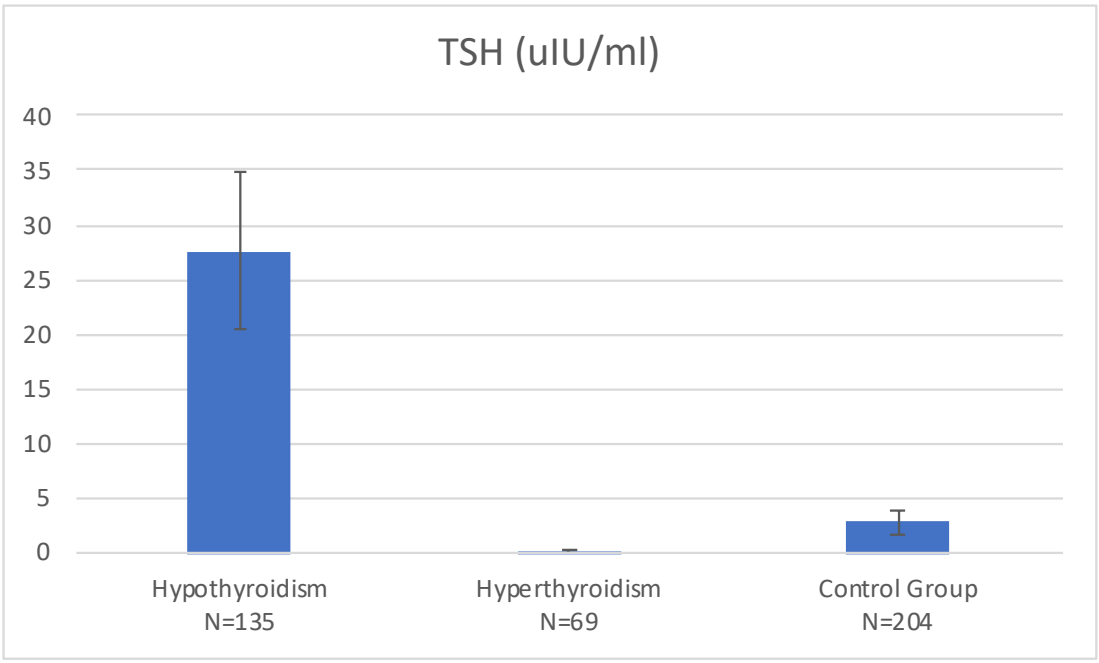

Figure 1: TSH (µIU/mL) levels in Hypothyroid and Control Groups

Hypothyroid patients showed markedly elevated TSH levels compared to healthy controls, indicating significant thyroid dysfunction ($p < 0.0001$).

Table 2: Oxidative Stress and Antioxidant Markers: Mean ± SD

Parameter	Hypothyroidism (n = 135)	Controls (n = 204)	p-value
MDA (nmol/L)	3.1 ± 0.9	1.07 ± 0.61	<0.0001
SOD (U/mL)	2.80 ± 0.11	3.42 ± 0.95	<0.0001
TAC (mmol/L)	0.72 ± 0.31	1.84 ± 0.21	<0.0001
Vitamin C (mg/dL)	0.91 ± 0.12	1.21 ± 0.11	<0.0001
Vitamin E (µg/dL)	0.66 ± 0.07	6.86 ± 1.03	<0.0001

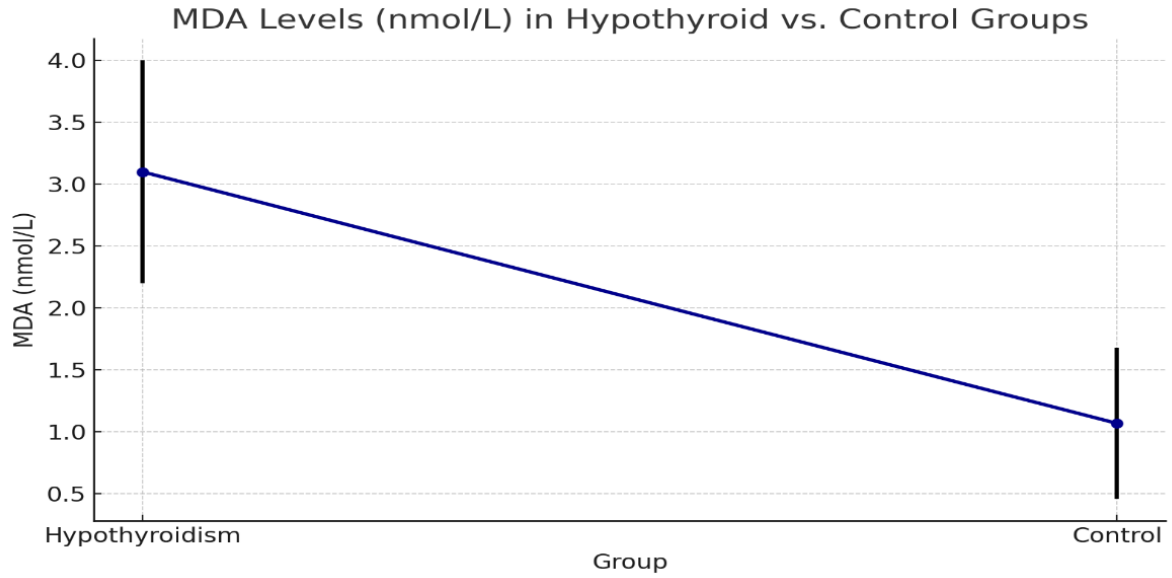

Figure 2: MDA levels in thyroid disorders

The line graph shows significantly higher malondialdehyde (MDA) levels in hypothyroid patients (3.1 ± 0.9 nmol/L) compared to controls (1.07 ± 0.61 nmol/L), indicating increased lipid peroxidation and oxidative stress ($p < 0.0001$).

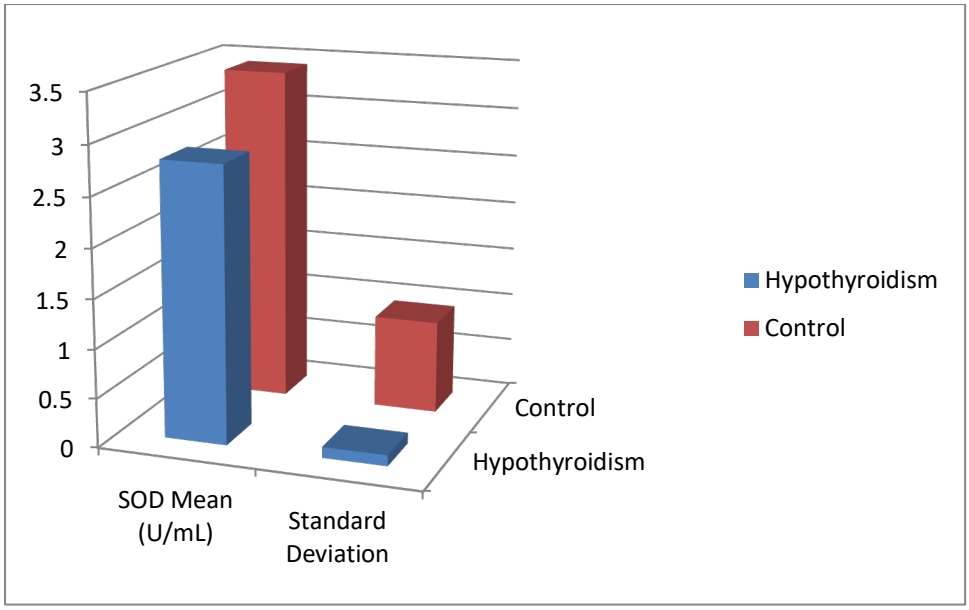

Figure 3: Superoxide Dismutase (SOD) Levels and Standard Deviation in Hypothyroid and Control Groups

The 3D bar chart shows that SOD levels were lower in hypothyroid patients (2.80 ± 0.11 U/mL) compared to controls (3.42 ± 0.95 U/mL), indicating reduced enzymatic antioxidant activity in hypothyroidism ($p < 0.0001$).

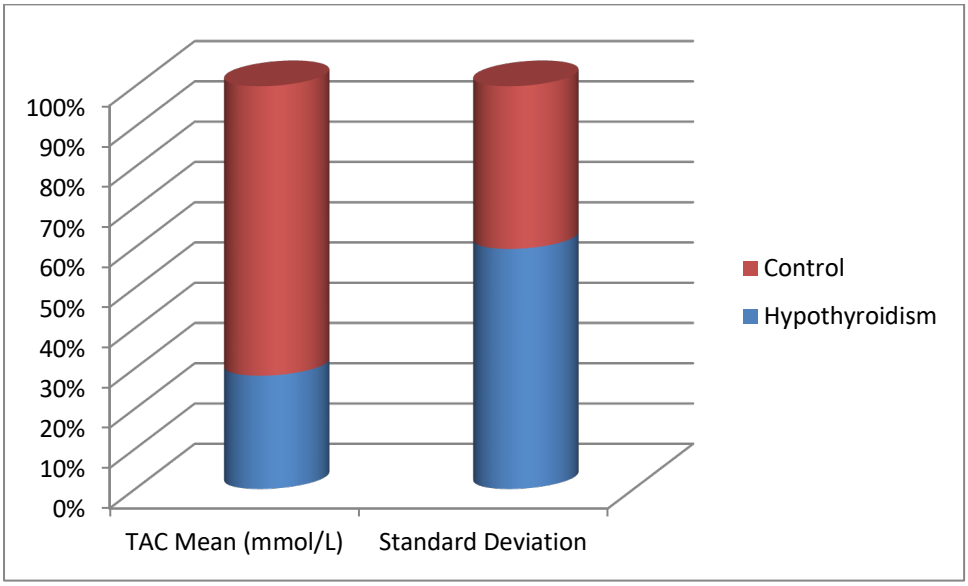

Figure 4: Total Antioxidant Capacity (TAC) in Hypothyroid and Control Groups

This 3D stacked column chart shows a significant reduction in TAC levels in hypothyroid patients compared to healthy controls. The control group contributed a greater proportion to both the mean TAC and its standard deviation, indicating better overall antioxidant status. The results emphasize impaired antioxidant defense in hypothyroid conditions ($p < 0.0001$).

Vitamin C and E comparisons

Table 3: Correlation between Hypothyroidism and Oxidative Stress Parameters

Marker	r Coefficient	95% CI	p-value
MDA	0.45	0.25 - 0.62	<0.001
SOD	-0.31	-0.48 --0.10	0.015
TAC	0.55	0.37 - 0.71	<0.001

- MDA had a moderate positive correlation with hypothyroid status, indicating elevated oxidative damage.
- SOD showed a negative correlation, reflecting weakened enzymatic defenses.
- TAC had a moderate positive correlation, possibly as a compensatory antioxidant mechanism.

Discussion

This study demonstrates that hypothyroidism is associated with increased oxidative stress and reduced antioxidant defenses in a Central Indian population.

A. Elevated Oxidative Stress in Hypothyroidism: We observed significantly higher malondialdehyde (MDA) levels in hypothyroid patients (3.1 ± 0.9 nmol/L) compared to controls, reflecting increased lipid peroxidation and cellular damage.

MDA also showed a moderate positive correlation with hypothyroidism (r = 0.45), confirming earlier findings that oxidative stress plays a role in thyroid hormone deficiency [5,6].

B. Antioxidant Depletion: Antioxidants including superoxide dismutase (SOD)[7,8], total antioxidant capacity (TAC), Vitamin C, and Vitamin E were significantly reduced in hypothyroid patients (all $p< 0.0001$). The drop-in SOD activity (r = -0.31) and low TAC (r = 0.55) suggest a disrupted antioxidant defense system and possible compensatory upregulation. These changes are consistent with prior studies reporting impaired redox homeostasis in thyroid dysfunction [9].

C. Pathophysiological and Clinical Implications: Oxidative imbalance may contribute to many systemic effects seen in hypothyroidism [10], including fatigue, weight gain, cognitive slowing, and cardiovascular risk. Persistent ROS exposure can damage lipids, proteins, and nucleic acids, compounding metabolic inefficiency. Importantly, low levels of Vitamin C and E-key non-enzymatic antioxidants-indicate dietary or metabolic insufficiency, and their supplementation may offer therapeutic benefit when paired with thyroid hormone replacement [11, 12, 13].

Limitations

- Single-center study
- No evaluation of post-treatment oxidative status
- Tissue-specific oxidative markers were not assessed
- Despite these, the large sample size and use of standardized biochemical methods strengthen the reliability of our results.

Conclusion

This study establishes that hypothyroidism is significantly associated with oxidative stress, marked by elevated malondialdehyde (MDA) levels and reduced antioxidant markers, including SOD, TAC, Vitamin C, and Vitamin E.

These biochemical alterations reflect a disrupted redox balance and may underlie many of the systemic complications of hypothyroidism.

Monitoring oxidative stress markers alongside thyroid function tests can enhance the understanding and management of hypothyroid disorders. Moreover, antioxidant supplementation may be considered as an adjunctive therapeutic approach, especially in patients with persistently elevated oxidative markers.

Further large-scale and longitudinal studies are needed to evaluate the clinical benefits of such interventions.

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