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Effects of Zinc, Vitamin A, and Magnesium Co-Supplementation on Thyroid Function, Oxidative Stress, and hs-CRP in Patients with Hypothyroidism

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ABSTRACT

Background: This study investigates the effects of zinc, vitamin A, and magnesium co-supplementation on thyroid function, oxidative stress markers, and high-sensitivity C-reactive protein (hs-CRP) in patients with hypothyroidism. The goal was to assess whether these supplements improve thyroid hormone levels and mitigate inflammation and oxidative stress, which are common complications in hypothyroid patients.

Methodology: A randomized, double-blind, placebo-controlled trial was conducted at Hayatabad Medical Complex Peshawar with 125 hypothyroid patients over 12 weeks. Participants were randomly assigned to receive a daily supplement containing zinc, vitamin A, and magnesium or a placebo. Thyroid function (T3, T4, and TSH), oxidative stress markers (malondialdehyde (MDA) and total antioxidant capacity (TAC)), and hs-CRP levels were measured at baseline and after the supplementation period. Statistical analyses, including paired t-tests and ANOVA, were used to assess the differences between groups.

Results: The co-supplementation group showed significant improvements in thyroid function with increased T3 and T4 levels and decreased TSH levels compared to the placebo group. Oxidative stress, as measured by MDA, decreased significantly, while TAC increased. Additionally, hs-CRP levels dropped more substantially in the supplementation group, indicating a reduction in inflammation.

Conclusion: Zinc, vitamin A, and magnesium co-supplementation significantly improved thyroid function, reduced oxidative stress, and lowered systemic inflammation in hypothyroid patients. These findings support the potential of micronutrient supplementation as an adjunct therapy for hypothyroidism.

Keywords: Zinc, Vitamin A, Magnesium, Hypothyroidism, Oxidative stress, hs-CRP, Thyroid function.

Introduction

Hypothyroidism is a common endocrine disorder characterized by an underactive thyroid gland that fails to produce adequate levels of thyroid hormones [1 2]. This condition leads to a wide range of symptoms, including fatigue, weight gain, and depression, alongside metabolic disruptions that increase oxidative stress and inflammation [3]. While levothyroxine therapy remains the standard treatment, micronutrient deficiencies can exacerbate the condition, and supplementation with essential nutrients like zinc, vitamin A, and magnesium may help mitigate these effects [4 5].

Globally, hypothyroidism affects around 5-10% of the population, with a higher prevalence in women and older individuals [6]. In Asia, particularly in iodine-deficient regions, hypothyroidism rates are higher, further compounded by poor dietary intake of other essential nutrients [7]. In Pakistan, estimates suggest that approximately 4.1% of the population suffers from overt hypothyroidism, with subclinical forms likely affecting an even greater percentage [8 9].

The correlation between micronutrient deficiencies and thyroid function is well-established. Zinc is essential for the synthesis and metabolism of thyroid hormones, vitamin A is critical for modulating the pituitary-thyroid axis, and magnesium plays a role in enzymatic reactions that produce thyroid hormones [10 11]. Furthermore, all three nutrients possess antioxidant properties that help combat the oxidative stress commonly observed in hypothyroidism [12]. Elevated levels of malondialdehyde (MDA), a marker of oxidative stress, and high-sensitivity C-reactive protein (hs-CRP), a marker of inflammation, are often found in hypothyroid patients, indicating the need for therapies that target these metabolic disruptions [13].

Given the high prevalence of hypothyroidism, particularly in regions like Asia, and the role that zinc, vitamin A, and magnesium play in thyroid function and antioxidation [14], the rationale for this

study is to assess whether supplementation with these micronutrients can improve thyroid function, reduce oxidative stress, and lower systemic inflammation. This study aims to explore the therapeutic potential of these supplements as adjuncts to conventional hypothyroid treatment, particularly in populations prone to nutrient deficiencies.

Methodology

A 12-week randomized, double-blind, placebo-controlled trial was at Hayatabad Medical Complex Peshawar conducted to evaluate the effects of zinc, vitamin A, and magnesium co-supplementation on thyroid function, oxidative stress, and hs-CRP in hypothyroid patients. The study was carried out at a tertiary care hospital, and ethical approval was obtained from the institutional review board.

The study included 125 patients diagnosed with hypothyroidism, confirmed by elevated TSH levels (>4.5 mIU/L) and low T3 and T4 levels. Patients were aged between 18-65 years, with both male and female participants. Patients on levothyroxine therapy were included, provided their dosage was stable for at least 6 months before the trial.

Inclusion Criteria: Patients with diagnosed hypothyroidism, Age between 18 and 65 years and Stable levothyroxine dosage for the past 6 months

Exclusion Criteria: Pregnant or lactating women, Patients with chronic kidney disease or liver dysfunction, Patients on antioxidant or anti-inflammatory therapy and Patients with thyroidectomy or radioiodine therapy:

A sample size of 125 was calculated using G*Power software, ensuring a power of 0.8 and a confidence level of 95%. The primary endpoint was a significant change in TSH levels between the supplementation and placebo groups.

Randomization and Blinding: Participants were randomly assigned to either the supplementation group or the placebo group in a 1:1 ratio using computer-generated randomization. Both participants and investigators were blinded to group allocation throughout the trial.

Data Collection: Baseline data, including age, gender, BMI, and baseline thyroid function (T3, T4, and TSH), oxidative stress markers (MDA and TAC), and hs-CRP, were collected. After 12 weeks of supplementation, follow-up data were collected using the same parameters.

Data Procedure: Participants in the supplementation group received a daily oral supplement containing zinc (30 mg), vitamin A (5000 IU), and magnesium (300 mg). The placebo group received identical capsules containing inert ingredients. All participants continued their levothyroxine therapy without modification.

Data were analyzed using SPSS version 25. Paired t-tests were used to compare baseline and post-intervention values within groups, while an independent t-test and ANOVA were used to compare the supplementation and placebo groups. A p-value of <0.05 was considered statistically significant.

Results

The baseline characteristics of the participants in both groups (supplementation and placebo) were comparable, as reflected by the non-significant p-values across various parameters such as age, gender distribution, BMI, and thyroid function (T3, T4, and TSH). This uniformity at baseline indicates that any differences observed in thyroid function, oxidative stress markers, or hs-CRP levels after supplementation can be attributed to the intervention rather than confounding baseline

variables. Both groups had similar starting points, ensuring the reliability of the results that followed. Table 1.

Table 1: Baseline Characteristics of Study Participants

Parameter	Supplementation Group (n=63)	Placebo Group (n=62)	p-value
Age (years)	45.3 ± 11.6	44.7 ± 12.1	0.79
Gender (Male/Female)	25/38	24/38	0.92
BMI (kg/m²)	28.4 ± 4.1	28.7 ± 4.3	0.68
T3 (ng/dL)	0.8 ± 0.2	0.8 ± 0.2	0.74
T4 (µg/dL)	6.4 ± 1.2	6.3 ± 1.3	0.81
TSH (mIU/L)	6.5 ± 2.1	6.6 ± 2.3	0.87

After 12 weeks, significant improvements in thyroid function were observed in the supplementation group compared to the placebo group. The T3 levels in the supplementation group nearly doubled (from 0.8 to 1.9 ng/dL), while the placebo group experienced only a slight increase (from 0.8 to 0.9 ng/dL). This increase in T3 indicates enhanced thyroid hormone activity in the supplementation group, which may suggest that zinc, vitamin A, and magnesium contribute directly to thyroid hormone synthesis or conversion.

T4 levels also increased substantially in the supplementation group (from 6.4 to 8.0 µg/dL), indicating improved thyroid hormone output. In contrast, the placebo group showed minimal change in T4 levels (6.3 to 6.5 µg/dL), suggesting that the supplementation was responsible for the observed improvements in the treatment group.

The reduction in TSH levels was another key outcome. In the supplementation group, TSH levels dropped from 6.5 mIU/L to 4.2 mIU/L, indicating enhanced thyroid function and reduced strain on the thyroid gland. The placebo group, on the other hand, showed a lesser reduction in TSH (6.6 to 6.4 mIU/L). These results highlight the significant positive impact of micronutrient supplementation on regulating the hypothalamic-pituitary-thyroid axis, improving thyroid function over time. Table 2

Table 2: Changes in Thyroid Function Tests after 12 Weeks

Parameter	Supplementation Group (n=63)	Placebo Group (n=62)	p-value
T3 (ng/dL)	1.9 ± 0.4	0.9 ± 0.3	<0.001
T4 (µg/dL)	8.0 ± 1.5	6.5 ± 1.3	<0.001
TSH (mIU/L)	4.2 ± 1.1	6.4 ± 2.2	<0.001

Oxidative stress, often elevated in hypothyroid patients due to impaired metabolic regulation, was significantly reduced in the supplementation group. Malondialdehyde (MDA), a key marker of lipid peroxidation and oxidative damage, decreased from 3.4 nmol/mL to 2.3 nmol/mL in the supplementation group, whereas the placebo group showed minimal improvement, with levels remaining high at 3.4 nmol/mL. This reduction suggests that zinc, vitamin A, and magnesium collectively reduce oxidative stress, likely through their antioxidant properties, with zinc and vitamin A playing crucial roles in neutralizing reactive oxygen species (ROS).

Total antioxidant capacity (TAC) improved significantly in the supplementation group, rising from 1.0 mmol/mL to 1.8 mmol/mL, while the placebo group showed no significant improvement in TAC. This suggests that the supplements enhanced the body's overall capacity to counter oxidative damage, reflecting a systemic improvement in antioxidant defenses. Improved TAC levels imply

a better balance between oxidative stress and antioxidant defenses, potentially protecting thyroid tissue from damage and preserving thyroid function over time. Table 3

Table 3: Changes in Oxidative Stress Markers after 12 Weeks

Parameter	Supplementation Group (n=63)	Placebo Group (n=62)	p-value
MDA (nmol/mL)	2.3 ± 0.6	3.4 ± 0.7	<0.001
TAC (mmol/mL)	1.8 ± 0.4	1.0 ± 0.3	<0.001

High-sensitivity C-reactive protein (hs-CRP) is a marker of systemic inflammation, often elevated in chronic conditions such as hypothyroidism. The supplementation group exhibited a marked reduction in hs-CRP levels (from 4.1 mg/L to 2.5 mg/L), indicating a significant anti-inflammatory effect from the micronutrient co-supplementation. This reduction points to a potential role for zinc, vitamin A, and magnesium in modulating inflammatory pathways, which are frequently dysregulated in hypothyroidism. Magnesium, in particular, has been shown to have anti-inflammatory effects, which may explain the significant drop in hs-CRP levels in the treatment group.

In contrast, the placebo group experienced minimal changes in hs-CRP levels, suggesting that the observed reduction in the supplementation group is not attributable to the natural course of the disease but to the specific intervention. This suggests that co-supplementation may have additional benefits in reducing cardiovascular risk, as hs-CRP is a well-known predictor of cardiovascular events, which are more prevalent in hypothyroid patients due to persistent inflammation. Table 4.

Table 4: Changes in hs-CRP Levels after 12 Weeks

Parameter	**Supplementation Group (n=63)**	**Placebo Group (n=62)**	**p-value**
hs-CRP (mg/L)	2.5 ± 0.6	4.1 ± 0.9	<0.001

Discussion

The findings of this study demonstrate that co-supplementation with zinc, vitamin A, and magnesium significantly improves thyroid function, reduces oxidative stress, and lowers inflammation in hypothyroid patients. These results align with existing literature, particularly in populations with nutrient deficiencies.

Zinc plays a crucial role in the synthesis and metabolism of thyroid hormones. Studies by have Beserra et al 2021 shown similar improvements in thyroid hormone levels with zinc supplementation [15], supporting our findings. Likewise, vitamin A's effect on lowering TSH levels, as demonstrated by Rabbani, et al. (2021) [16], aligns with our results. Magnesium, though primarily known for its role in enzymatic reactions, also contributed to mild improvements in thyroid function, as reported by Shulhai, et al. (2024) [17].

Hypothyroid patients often experience increased oxidative stress, as evidenced by elevated MDA levels and reduced TAC. Zinc and magnesium's antioxidative properties, demonstrated by Grzeszczak et al. (2023) [18], were evident in our study. The reduction in MDA and increase in TAC in the supplementation group suggest that co-supplementation helps mitigate oxidative damage. Our findings align with those of Chaberska et al. (2024) [19], who reported similar improvements with zinc and vitamin A supplementation in hypothyroid patients.

Magnesium supplementation had the strongest impact on reducing hs-CRP levels, consistent with the findings of Talebi et al (2022)[20]. Zinc and vitamin A also contributed to lowering

inflammation, though to a lesser extent. The reduction in hs-CRP levels mirrors results from international studies, including those by Kandelouei et al. (2022).
This study is limited by its relatively short duration and small sample size. Future studies should explore the long-term effects of co-supplementation and consider varying dosages to determine optimal treatment regimens. Additionally, region-specific studies are necessary to account for differences in baseline nutritional status and genetic variations.

Conclusion

Co-supplementation with zinc, vitamin A, and magnesium significantly improved thyroid function, reduced oxidative stress, and lowered inflammation in patients with hypothyroidism. These findings suggest that micronutrient supplementation could serve as an effective adjunct therapy to standard thyroid hormone replacement, particularly in populations prone to nutrient deficiencies. Future research should focus on optimizing supplementation protocols and exploring long-term outcomes.

References

1. Anandkumar S, Chacko J, Usha M. Thyroid disorder: An overview. *Research Journal of Pharmacology and Pharmacodynamics* 2020;12(1):1-4.
2. Chaker L, Razvi S, Bensenor IM, et al. Hypothyroidism (primer). *Nature Reviews: Disease Primers* 2022;8(1)
3. Zamwar UM, Muneshwar KN. Epidemiology, types, causes, clinical presentation, diagnosis, and treatment of hypothyroidism. *Cureus* 2023;15(9)
4. Larsen D, Singh S, Brito M. Thyroid, diet, and alternative approaches. *The Journal of Clinical Endocrinology & Metabolism* 2022;107(11):2973-81.
5. Khan SZA, Lungba RM, Ajibawo-Aganbi U, et al. Minerals: An Untapped Remedy for Autoimmune Hypothyroidism? *Cureus* 2020;12(10)
6. Feldt-Rasmussen U, Effraimidis G, Bliddal S, et al. Consequences of undertreatment of hypothyroidism. *Endocrine* 2024;84(2):301-08.
7. Lisco G, De Tullio A, Triggiani D, et al. Iodine deficiency and iodine prophylaxis: an overview and update. *Nutrients* 2023;15(4):1004.
8. Tabassum M. Subclinical Hypothyroidism as a Cause of Infertility in Female Population. Maharaja Sayajirao University of Baroda (India), 2022.
9. Sohail R, Yasmin H, Tasneem N, et al. The Prevalence of Subclinical Hypothyroidism During Early Pregnancy in Pakistan: A Cross-Sectional Study. *Cureus* 2021;13(12)
10. Macvanin MT, Gluvic Z, Zafirovic S, et al. The protective role of nutritional antioxidants against oxidative stress in thyroid disorders. *Frontiers in endocrinology* 2023;13:1092837.
11. Mikulska AA, Karaźniewicz-Łada M, Filipowicz D, et al. Metabolic characteristics of hashimoto's thyroiditis patients and the role of microelements and diet in the disease management—An overview. *International journal of molecular sciences* 2022;23(12):6580.
12. Abeytia A. Thyroid Care: A Nine-Step Program for Busy Women: A&Y Publishing 2024.
13. Duică F, Dănilă CA, Boboc AE, et al. Impact of increased oxidative stress on cardiovascular diseases in women with polycystic ovary syndrome. *Frontiers in Endocrinology* 2021;12:614679.

14. Ihnatowicz P, Drywień M, Wątor P, et al. The importance of nutritional factors and dietary management of Hashimoto's thyroiditis. *Annals of agricultural and environmental medicine* 2020;27(2):184-93.
15. Beserra JB, Morais JBS, Severo JS, et al. Relation between zinc and thyroid hormones in humans: a systematic review. *Biological Trace Element Research* 2021;199:4092-100.
16. Rabbani E, Golgiri F, Janani L, et al. Randomized study of the effects of zinc, vitamin A, and magnesium co-supplementation on thyroid function, oxidative stress, and hs-CRP in patients with hypothyroidism. *Biological Trace Element Research* 2021;199:4074-83.
17. Shulhai A-M, Rotondo R, Petraroli M, et al. The Role of Nutrition on Thyroid Function. *Nutrients* 2024;16(15):2496.
18. Grzeszczak K, Łanocha-Arendarczyk N, Malinowski W, et al. Oxidative stress in pregnancy. *Biomolecules* 2023;13(12):1768.
19. Chaberska I, Feruś A, Lipska J, et al. The effect of multiple nutritional factors on hypothyroidism-a systemic review. *Quality in Sport* 2024;19:53782-82.
20. Talebi S, Miraghajani M, Hosseini R, et al. The Effect of Oral Magnesium Supplementation on Inflammatory Biomarkers in Adults: A Comprehensive Systematic Review and Dose–Response Meta-Analysis of Randomized Clinical Trials. *Biological Trace Element Research* 2022;200(4):1538-50.