Influence of Zinc, Vitamin A and Magnesium supplementation on Hypothyroidism

When the thyroid gland fails to generate and release enough thyroid hormone into the bloodstream, hypothyroidism occurs. The metabolism activity will consequently slow down, often referred as thyroid dysfunction. Hypothyroidism symptoms includes: feel worn out, gain weight, or have problems adjusting to the cold. Micronutrient deficits, including those in zinc, magnesium, and vitamin A, can lead to hypothyroidism. The goal of this investigation was to ascertain how these micronutrient supplements affected hypothyroid patients. Edema, thin, brittle hair, goiter, peripheral, delayed relaxation of deep tendon reflexes, and dry skin are all signs of hypothyroidism. The production, metabolism, and action of thyroid hormones are all negatively impacted by zinc deficiency, which has been identified as a crucial component for maintaining adequate thyroid homeostasis. There has been a rise in oxidative stress linked to the pathophysiology of ATD, and Antioxidant vitamin A reduces the overproduction of free radicals. As the body's fourth most prevalent cation, magnesium (Mg) is a crucial cofactor in many enzymatic processes, including those involving the majority of the numerous Ion transporters connected to ATPases. Additionally; it has a direct impact on mitochondrial oxidative metabolism. Mg is therefore essential for energy metabolism. Supplementing with vitamin A, magnesium, and zinc may be helpful for those with hypothyroidism and for people with conditions linked to hyperthyroidism

Keywords: Magnesium, Zinc, Vitamin A, Thyroid Function, Hypothyroidism

INTRODUCTION

When the thyroid gland does not generate enough of the hormone thyroxin to satisfy the body's metabolic requirements, the condition is known as hypothyroidism. Hypothyroidism has also been related to insufficient consumption of certain minerals as zinc, magnesium, or vitamin A. Interleukin-2, lithium, interferon Alfa, tyrosine kinase inhibitors, and amiodarone are only few of the conventional medications that have been associated with thyroid dysfunction (Barbesino, 2020; López *et al*. 2021).If the hypothyroidism is not treated it can cause many problems like neuromuscular dysfunction, dyslipidemia, cognitive impairment, hypertension and infertility. (Hollowell *et al.* 2002). Age-related increases in the prevalence of hypothyroidism are more prevalent in women than in men (Boucai *et al*. 2021). Hypothyroidism may be brought on by a number of different things, such as autoimmune diseases, radiation treatment, thyroid surgery, drugs, or even congenital problems. Hypothyroidism (low levels of thyroid hormone) is most often caused by the Hashimoto's thyroiditis, in which the thyroid gland is attacked and destroyed by the immune system. Graves' disease and atrophic thyroiditis are two further examples of autoimmune conditions that may lead to hypothyroidism (Feldt-Rasmussen &Klose, 2016; Singer, 2017).

In order to identify SH (subclinical hypothyroidism), the concentrations of TSH (thyroid stimulating hormone) should be tested at least twice in a completely separate setting. Recently, SH (subclinical hypothyroidism) was categorized as mild, also known as grade 1. In grade 2, when the TSH level is over 9.9 mU/L but still within the reference range, severe hypothyroidism is indicated. A TSH level that is more than 10mU/L is considered very severe (Zhang *et al*. 2021).

Hypothyroidism symptoms may be affected by the severity of the condition as well as the patient's age. Adults may have a wide variety of some of the symptoms include fatigue, weight gain, cold sensitivity, constipation, dry skin, hair loss, and depression. Hoarseness, menstruation abnormalities, muscular weakness, and joint discomfort are some of the other symptoms that may be present (Dunn & Turner, 2016; Santos *et al.* 2022).

Some estimates place the number of people with an iodine shortage at more than a third of the global population (Kandi&Rao, 2022).Iodine is essential in the synthesis, maintenance, and generation of T3 and T4, the two hormones that regulate the thyroid (Rhee&Bhan, 2022).Hypothyroidism affects around 4–5% of the population throughout the globe (Hollowell *et al*. 2022; Hoogendoorn *et al*. 2016).The incidence of hypothyroidism in Pakistan's adult population is 4.1%, while the prevalence in children is 5.4%(Narayana *et al.* 2021).Due to the prevalence of autoimmune thyroid illness, hypothyroidism in adults is often caused by immunological dysfunction or minor shortages of micronutrients, both of which result in aberrant thyroid hormone production(OBA& KIMURA, 2017; Brown *et al.* 2020).

The production and metabolism of TSH are both reliant on the availability of a large number of trace elements in order to maintain normal thyroid function(Nazifi *et al*. 2019).The relationship between TSH and Zn has been studied extensively(Leblondel *et al*.2017; Freake *et al*. 2021).A zinc shortage has been linked to some endocrine diseases as well as detrimental effects on brain function, which are noticed in humans, particularly during the development stage(Kwan *et al*.2017; Georgieff, 2017).Zinc is a trace element that is involved in a wide range of physiological processes, including the immune system's function, DNA synthesis, and protein synthesis. An essential element is zinc. It is crucial for the synthesis and release of thyroid hormones, therefore it also has a significant impact on the thyroid's functionality. A lack of zinc has been linked to both decreased thyroid function and hypothyroidism (Severo *et al.* 2019).

Zn deficiency has been shown to have a lowering influence on TSH, but supplementing with Zn has been shown to have the opposite effect (KasimBaltaci *et al.*2017; Blatanc*ies et al.,*2014).Suggested a connection between zinc and thyroid stimulating hormone (TSH). According to the findings of a recent study, patients with hypothyroidism who took zinc supplements had elevated TSH levels(Kandhro *et al.* 2018).When it comes to maintaining healthy brain function, zinc is a crucial divalent metal ion that is abundant in the central nervous system(Gower-Winter & Levenson, 2022).Supplemental zinc may counteract the negative effects of zinc deficiency on cancer and other diseases when these outcomes have been linked to increased oxidants, cellular damage, and altered antioxidant defenses. Zn also has antioxidant properties. Oxidants tend to rise in concentration when zinc levels are low (Oteiza, 2022).

Vitamin A is an antioxidant that lowers the body's overall rate of producing potentially harmful free radicals (El-Laithy *et al*. 2016) Moreover, elevated Oxidative stress levels have been proven to affect the pathogenesis of ATD(Kawicka & Regulska-Ilow, 2015).Vitamin A deficiency (VAD), often known as a shortage of this nutrient, has been linked to lower levels of thyroidal iodine, which may have consequences for the pituitary-thyroid axis. Thyroid enlargement, trouble making thyroglobulin (Tg) and insufficient iodotyrosine coupling to produce T4 and T3 are all signs of this disorder. As a consequence, the risk of developing hypothyroidism is greater among populations consuming a diet low in both vitamin A and iodine than in those consuming a diet poor in just iodine (Biebinger *et al.*2017).

The mineral magnesium is crucial for a wide range of bodily functions. Some of these functions include the metabolism of energy, the synthesis of protein, and the creation of DNA. Thyroid function is dependent on its presence since it is required for the synthesis and release of thyroid hormones. A lack of magnesium has been linked to both reduced thyroid function and the condition known as hypothyroidism (Lall, 2022).

In hypothyroidism status thyroid gland does not produce enough of thyroxin hormone to meet the body's metabolism requirements. Hypothyroidism has also been related to insufficient consumption of certain minerals as zinc, magnesium, or vitamin A .(two lines were omit because it were repeated before). Some studies have linked dietary deficiencies in these crucial elements to thyroid dysfunction, underscoring the potential significance of correcting nutritional imbalances in the context of managing hypothyroidism (Barbesino, 2020; López*et al.* 2021). In this study we are giving dietary supplements because these supplements contain zinc, vitamin A and magnesium which are highly acceptable for the treatment of hypothyroidism (Oteiza, 2022).Thus, this study's objective was to identify the effect of zinc, vitamin A and magnesium on hypothyroidism. This study will help to improve nutrition education and policies to create awareness among patients suffering from hypothyroidism.

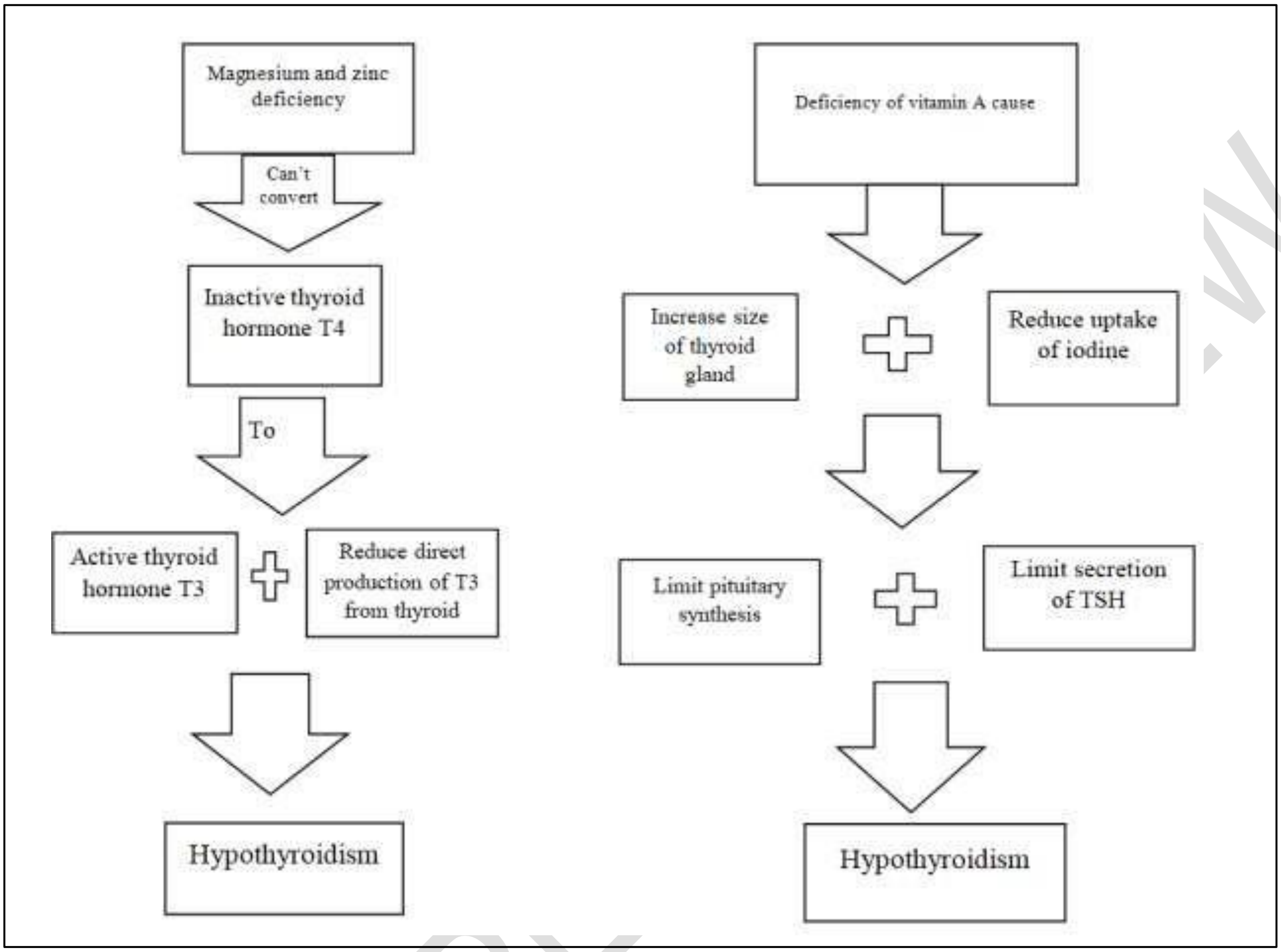

Figure1: Mechanism of Zinc. Vitamin A and Magnesium supplementation on Hypothyroidism

Experimental Designs **(need a reference for this figure).**

In a study carried out in 2021 by Rabbani and colleagues, hs-CRP levels, oxidative stress, and thyroid function in hypothyroid patients were studied in relation to the effects of these micronutrient supplements. 86 hypothyroid patients between the ages of 20 and 65 were randomly assigned to either the intervention group (n = 43), which received daily supplementation with one 30 mg zinc gluconate capsule, one 250 mg magnesium oxide tablet, and one 25,000 IU vitamin A capsule twice weekly for 10 weeks, or the placebo group (n = 43), which received exactly the same amount of placebo capsules and tablets for the same length of time. The diets and exercise routines of neither group were altered. Serum hs-CRP, anthropometric measurements (height and weight), oxidative markers (malondialdehyde (MDA) and total antioxidant capacity (TAC), thyroid hormones (free and total thyroxin (FT4 and TT4), free triiodothyronine (FT3), and thyroid-stimulating hormone (TSH) were all assessed at the start and end of the study. They found a significant increases in serum FT4, decreases in anthropometric indices, and decreased levels of serum hs-CRP in the intervention group by the end of the 10-week process (P 0.05). After the intervention, serum TSH, FT3, TT4, and MDA did not significantly alter in the placebo group, whereas serum TAC and hs-CRP did (P 0.05). Patients with hypothyroidism and conditions linked to hyperthyroidism may benefit from taking supplements of zinc, vitamin A, and magnesium. (Rabbani, *et al.* 2021)

In 2016, Aziz MA conducted a study that aimed to examine the relationship between serum levels of Interleukin-6, tumor necrosis factor, thyroxin, triiodothyronine, and thyroid-stimulating hormone in hypothyroid individuals. The study included 27 hypothyroid patients and 27 healthy controls. The findings showed that hypothyroidism patients' serum levels of zinc, interleukin-6, and tumor necrosis factor were considerably lower (p 0.05) than those of the control group. Patients with hypothyroidism significantly lower (p 0.05) compared to the control group's values. After receiving zinc, the patient group's "interleukin-6 and tumor necrosis factor" levels significantly increased (p 0.05) when compared to the control group. (Aziz, et al. 2016)

The study was conducted in 2007, in this study, zinc deficiency can lead to lower levels of thyroid hormones and a slower resting metabolic rate (RMR). Zinc is essential for optimal thyroid hormone metabolism. This study aimed to evaluate the effects in zinc-deficient, active women on the effects of zinc supplementation on serum ferritin, plasma total triiodothyronine (T3), plasma free T3 and T4, plasma total triiodothyronine (T4), plasma thyroid-stimulating hormone, and RMR. The aforementioned measurements were taken at 0, 2, and 4 months after two female college students who were zinc deficient (ZD1 and ZD2) received 26.4 mg/day of zinc (as zinc gluconate). Despite receiving treatment for their clinical zinc deficiency, both subjects' blood ferritin levels dropped, placing them in the same group. The levels of thyroid hormones, particularly total T3 and RMR, seemed to be improved by zinc supplementation. (Maxwell, *et al* .2007)

In 2008, researchers In Turkey's iodine-rich Ankara governorate, undertook the current investigation to assess the serum levels of selenium, magnesium, zinc and copper in individuals with subclinical hypothyroidism. These patients' responses to hormone replacement therapy were investigated as well as a result of its effects on these elements. Iron and selenium baseline levels in patients were considerably lower than that in the control group (67.7 10.4 vs. 83.7 17.3 g/dl; 55.7 38 vs. 275.7 24;
P = 0.03 g/dl, respectively). The patient group showed significantly higher serum magnesium levels (2.16 0.31 vs. 1.95 0.13 mg/dl, P 0.0001). Selenium levels or hsCRP showed a link (r = 0.408, p = 0.007). HsCRP levels were significantly higher in patients with selenium levels 80 g/l (n = 31) than in people who have selenium levels >80 g/l (n = 12; 1.99 g/l vs. 1.02 g/l; p = 0.014). When compared to pretreatment values, Ineuthyroid patients with SH, none of these biochemical risk variables and minor components have changed. Selenium deficiency may increase these patients' risk of cardiovascular disease. (Erdal *et al*. 2008).

Selenium and iron base levels were significantly lower in the sick group (67.7 10.4 vs. 83.7 17.3 g/dl and 55.7 38 vs. 275.7 24; P = 0.03 g/dl, respectively) than in the control group. Serum magnesium levels in the patient group were substantially higher (2.16 0.31 vs. 1.95 0.13 mg/dl, P 0.0001). HsCRP and selenium levels were linked (r = 0.408, p = 0.007). Those with selenium levels 80 g/l (n = 31) had substantially higher levels of HsCRP than those with selenium levels >80 g/l (n = 12; 1.99 g/l vs. 1.02 g/l; p = 0.014). None of these biochemical risk variables and trace elements had changed in euthyroid patients with SH when compared to pretreatment values. The risk of cardiovascular disease in these patients may increase due to selenium insufficiency. (Gupta, et al. 2010)

Another study was conducted in 2012, In comparison to unexposed controls, When exposed to 3,4,3′,4′ -tetrachlorobiphenyl while being fed a diet low in vitamin A, poultry chicks developed hypothyroidism. Food intake, the rate of metabolism, total serum thyroxine, total serum triiodothyronine, and thyroid weight all considerably increased. Surprisingly, the diet had no effect on the rate of growth. In chicks fed a low vitamin A— the hypothyroid response appeared to be inhibited in rats fed a low-iodine semi-purified diet and exposed to the PCB congener. The metabolic rate and percentage of free T3 (i.e., T3 resin uptake) increased in exposed chicks compared to controls, while total blood thyroxine and thyroid weight remained identical. While on this diet, serum retinol, growth rate, and food intake all fell. These findings imply that (i) blood levels of retinol may have influenced growth rate and (ii) vitamin A deficiency may have increased the likelihood that birds may experience PCB-induced hypothyroidism. (Spear, *et al*. 2012)

Subclinical hypothyroidism does influence fertility, found to a 2018 study. Women tend to have subclinical hypothyroidism 10–15 times more often than men do. Trace elements and other chemical elements are crucial for thyroid and fertility health. In order to ascertain whether there are any notable changes between the chemical element composition of male and female thyroids, as well as how these variations may be connected to the etiology of subclinical hypothyroidism, this study examined the chemical element composition of male and female thyroids. Twenty chemical elements were examined in the thyroid tissue of 105 people in good health (33 females and 72 males), including Al, B, Ba, Br, Ca, Cl, Cu, I, Fe, K, Li, Mg, Mn, Na, S, P, Si, Sr, and Zn. The mean levels of Al, B, Fe, Cu, Ca, Li, Mg, S, and Zn in female thyroid tissue were found to be lower than those in male thyroid tissue before the age of 40. The levels of Ba, Br, and Si in female thyroid gland tissue.(Zaichick, *et al*.2018)

Table 1:Original studies regarding influence of Zinc, Vitamin A and Magnesium supplementation on Hypothyroidism

Sr.no	Study subjects	Dietary intervention	Duration of the treatment	Treatment effect	References
1	84 healthy women's aged 17 to 50 years	Vitamin A supplementation	4months	Reduction in T4 value	(Farhangi *et al*. 2016)
2	50 patients of hypothyroidism aged 20 to 50 years	Zinc and magnesium supplementation	2 months	Improve magnesium and zinc level	(Un Nisa *et al* . 2013)
3	67 patients of hypothyroidism	Zinc supplementation	1 months	Positively correlation of serum zinc level with thyroid	(Ertek *et al* .2010)
4	60 male ad 72 female patients	Zinc supplementation	6 months	Zinc status and serum thyroid hormone level were improved	(Kandhro, 2009)
5	50 hypothyroid patients and 28 healthy participants	Zn, Cu, Se, Mn and Mg supplementation	2 weeks	TSH levels and lipids (cholesterol, triglycerides, and very low density lipoproteins) have a good relation.	(Rashid *et al* . 2010)
6	30 adult male rats	Zinc supplementation	4 months	variations in several elements' serum levels in rats	(Baltaci, 2013)
7	40 normal healthy subjects and 40 subjects with thyroid hormone	Magnesium, calcium and phosphorous supplementation	4 weeks	Magnesium, calcium and phosphorus level were Improved	(Sridevi,2016)
8	60 patients of hypothyroidism	Vitamin A supplementation	6 weeks	Vitamin A have effect on thyroid hormone	(Coustaut,2010)
9	50 patients of hypothyroidism	Magnesium supplementation	4 weeks	Magnesium level were improved	(Wang,2018)

CONCLUSIONS

When the thyroid does not produce (words were omit not need same mean) enough thyroid hormone into the bloodstream, hypothyroidism develops. Micronutrient deficits, including those in zinc, magnesium, and vitamin A, can lead to hypothyroidism. This study's goal was to ascertain how these micronutrient supplements affected hypothyroid patients. Edema, thin, brittle hair, goiter, peripheral, delayed relaxation of deep tendon reflexes, and dry skin are all signs of hypothyroidism. Mg is therefore essential for energy metabolism. Supplementing with zinc, vitamin A, and magnesium may be helpful for those with hypothyroidism and for people with conditions linked to hyperthyroidism.

Supplementary materials

Not applicable.

Institutional Review Board Statement

The study was approved by the Bioethical Committee of the University of Lahore

Informed Consent Statement

Not applicable.

Data Availability Statement

All of the data is included in the article/Supplementary Material.

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