



Influence of Zinc, Vitamin A and Magnesium supplementation on Hypothyroidism

Ghulam Rubab, Syeda Mashal Hassan, Areeba Sanaullah, Shahnai Basharat, Misbah Arshad and Momina Shahid

The University of Lahore, Lahore, Pakistan

*Correspondence: fatimamishbah10@gmail.com Received 19 Aug., 2023, Revised: 23 September 2023, Accepted: 25 September 2023 e-Published: 30 September 2023

When the thyroid fails to generate and release enough thyroid hormone into the bloodstream, hypothyroidism occurs. Your metabolism will consequently slow down. You may have hypothyroidism, often referred to as a thyroid dysfunction, if you 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 males. (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 (Kasim Baltaci et al. 2017; Blatancies 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).

Hypothyroidism is a disorder in which the thyroid gland does not produce enough of the hormone thyroxin to meet the needs of the body's metabolism. Hypothyroidism has also been related to insufficient consumption of certain minerals as zinc, magnesium, or vitamin A. Hypothyroidism prevalence in Pakistani adult population is 4.1%, while children have a prevalence of 5.4% (Narayana & Woods 2021). 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.

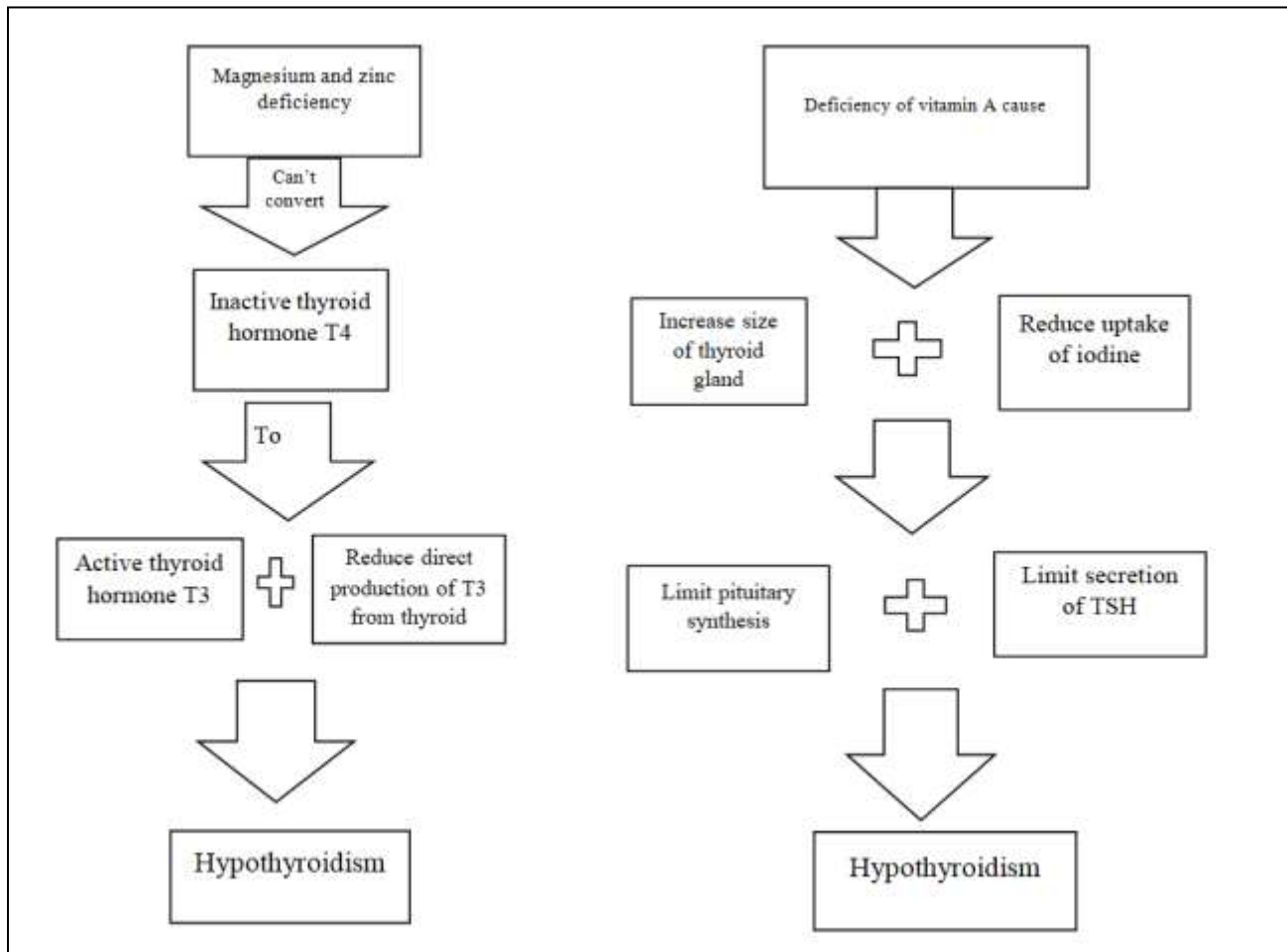


Figure1: Mechanism of Zinc, Vitamin A and Magnesium supplementation on Hypothyroidism

Experimental Designs

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. We found 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 area, 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, in euthyroid 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 and release 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.

Author contributions

The article work was done under the supervision of Dr. Shahnai Basharat., Misbah Arshad and Momina Shahid. Abstract writing, introduction, results were done by Mashal and Ghulam Rubab. The rephrasing and formatting was done by Areeba. All authors read and approved the final version.

Funding statement

This study was supported by the authors.

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.

Acknowledgments

I would also like to acknowledge the efforts of our supervisor **Dr. Shahnai Basharat**, without whom this could not be possible. I would like to thank the faculty of my department which helped me throughout this journey.

Conflict of interest

The authors declare no conflict of interest.

Copyrights: © 2023@ author (s).

This is an **open access** article distributed under the terms of the **Creative Commons Attribution License (CC BY 4.0)**, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use,

distribution or reproduction is permitted which does not comply with these terms.

Publisher's note/Disclaimer

All claims stated in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher. ISISnet remains neutral with regard to jurisdictional claims in published maps and institutional affiliations. ISISnet and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

Peer Review: ISISnet follows double blind peer review policy and thanks the anonymous reviewer(s) for their contribution to the peer review of this article.

REFERENCES

- Aziz, M. A., Habil, N. Y., & Diab, A. K. S. (2016). Effectiveness of zinc supplementation in regulating serum hormonal and inflammatory status in hypothyroidism patients. *Med. J. Babylon*, 13, 347-353.
- Baltaci, A. K., Mogulkoc, R., & Belviranli, M. (2013). Serum levels of calcium, selenium, magnesium, phosphorus, chromium, copper and iron--their relation to zinc in rats with induced hypothyroidism. *Acta Clin Croat*, 52(2), 151-156.
- Baltaci, A. K., Mogulkoc, R., Kul, A., Bediz, C. S., & Ugur, A. (2004). Opposite effects of zinc and melatonin on thyroid hormones in rats. *Toxicology*, 195(1), 69-75.
- Barbesino, G. (2010). Drugs affecting thyroid function. *Thyroid*, 20(7), 763-770.
- Betsy, A., Binitha, M. P., & Sarita, S. (2013). Zinc deficiency associated with hypothyroidism: an overlooked cause of severe alopecia. *International journal of trichology*, 5(1), 40.
- Biebinger, R., Arnold, M., Langhans, W., Hurrell, R. F., & Zimmermann, M. B. (2007). Vitamin A repletion in rats with concurrent vitamin A and iodine deficiency affects pituitary TSH β gene expression and reduces thyroid hyperstimulation and thyroid size. *The Journal of nutrition*, 137(3), 573-577.
- Boucai, L., Hollowell, J. G., & Surks, M. I. (2011). An approach for development of age-, gender-, and ethnicity-specific thyrotropin reference limits. *Thyroid*, 21(1), 5-11.
- Brown, N. S., Smart, A., Sharma, V., Brinkmeier, M. L., Greenlee, L., Camper, S. A., ... & Haugen, B. R. (2000). Thyroid hormone resistance and increased metabolic rate in the RXR- γ -deficient mouse. *The Journal of clinical investigation*, 106(1), 73-79.

- Chen, S. M., Kuo, C. D., Ho, L. T., & Liao, J. F. (2005). Effect of hypothyroidism on intestinal zinc absorption and renal zinc disposal in five-sixths nephrectomized rats. *The Japanese journal of physiology*, 55(4), 211-219.
- Coustaut, M., Pallet, V., Garcin, H., & Higuieret, P. (1996). The influence of dietary vitamin A on triiodothyronine, retinoic acid, and glucocorticoid receptors in liver of hypothyroid rats. *British Journal of Nutrition*, 76(2), 295-306.
- El-Laithy, N. A., Badawy, E. A., Youness, E. R., Ibrahim, A. M., El Nemr, M., & El-Shamy, K. A. (2016). Antioxidant defense system as a protector against oxidative stress induced by thyroid dysfunction. *Der Pharmacia Lettre*, 8, 113-118.
- Erdal, M., Sahin, M., Hasimi, A., Uckaya, G., Kutlu, M., & Saglam, K. (2008). Trace element levels in hashimoto thyroiditis patients with subclinical hypothyroidism. *Biological trace element research*, 123, 1-7.
- Ertek, S., Cicero, A. F., Caglar, O., & Erdogan, G. (2010). Relationship between serum zinc levels, thyroid hormones and thyroid volume following successful iodine supplementation. *Hormones*, 9(3), 263-268.
- Ertek, S., Cicero, A. F., Caglar, O., & Erdogan, G. (2010). Relationship between serum zinc levels, thyroid hormones and thyroid volume following successful iodine supplementation. *Hormones*, 9(3), 263-268.
- Farhangi, M. A., Javid, A. Z., & Dehghan, P. (2016). The effect of enriched chicory inulin on liver enzymes, calcium homeostasis and hematological parameters in patients with type 2 diabetes mellitus: a randomized placebo-controlled trial. *Primary care diabetes*, 10(4), 265-271.
- Freake, H. C., Govoni, K. E., Guda, K., Huang, C., & Zinn, S. A. (2001). Actions and interactions of thyroid hormone and zinc status in growing rats. *The Journal of nutrition*, 131(4), 1135-1141.
- Freake, H. C., Govoni, K. E., Guda, K., Huang, C., & Zinn, S. A. (2001). Actions and interactions of thyroid hormone and zinc status in growing rats. *The Journal of nutrition*, 131(4), 1135-1141.
- Gaitonde, D. Y., Rowley, K. D., & Sweeney, L. B. (2012). Hypothyroidism: an update. *South African Family Practice*, 54(5), 384-390.
- Georgieff, M. K. (2007). Nutrition and the developing brain: nutrient priorities and measurement. *The American journal of clinical nutrition*, 85(2), 614S-620S.
- Gower-Winter, S. D., & Levenson, C. W. (2012). Zinc in the central nervous system: from molecules to behavior. *Biofactors*, 38(3), 186-193.
- Gröber, U., Schmidt, J., & Kisters, K. (2015). Magnesium in prevention and therapy. *Nutrients*, 7(9), 8199-8226.
- Gupta, R. P., P. C. Verma, and S. L. Garg. "Effect of experimental zinc deficiency on thyroid gland in guinea-pigs." *Annals of nutrition and metabolism* 41.6 (1997): 376-381.
- Hollowell, J. G., Staehling, N. W., Flanders, W. D., Hannon, W. H., Gunter, E. W., Spencer, C. A., & Braverman, L. E. (2002). Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *The Journal of Clinical Endocrinology & Metabolism*, 87(2), 489-499.
- Hollowell, J. G., Staehling, N. W., Flanders, W. D., Hannon, W. H., Gunter, E. W., Spencer, C. A., & Braverman, L. E. (2002). Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *The Journal of Clinical Endocrinology & Metabolism*, 87(2), 489-499.
- Hoogendoorn, E. H., Hermus, A. R., De Vegt, F., Ross, H. A., Verbeek, A. L., Kiemeneij, L. A., ... & den Heijer, M. (2006). Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: s of age and sex. *Clinical chemistry*, 52(1), 104-111.
- Hsu, J. M., Root, A. W., Duckett, G. E., Smith Jr, J. C., Yunice, A. A., & Kepford, G. (1984). The effect of magnesium depletion on thyroid function in rats. *The Journal of nutrition*, 114(8), 1510-1517.
- Kandhro, G. A., Kazi, T. G., Afridi, H. I., Kazi, N., Arain, M. B., Sarfraz, R. A., ... & Shah, A. Q. (2008). Evaluation of iron in serum and urine and their relation with thyroid function in female goitrous patients. *Biological trace element research*, 125(3), 203-212.
- Kandhro, G. A., Kazi, T. G., Afridi, H. I., Kazi, N., Baig, J. A., Arain, M. B., ... & Syed, N. (2009). Effect of zinc supplementation on the zinc level in serum and urine and their relation to thyroid hormone profile in male and female goitrous patients. *Clinical Nutrition*, 28(2), 162-168.
- Kandi, S., & Rao, P. (2012). Anti-thyroid peroxidase antibodies: Its effect on thyroid gland and breast tissue. *Annals of Tropical Medicine & Public Health*, 5(1).
- Kasim Baltaci, A., Mogulkoc, R., Seref Bediz, C., Kul, A., & Ugur, A. (2003). Pinealectomy and zinc deficiency have opposite effects on thyroid hormones in rats. *Endocrine research*, 29(4), 473-481.
- Kawicka, A., & Regulska-Ilow, B. (2015). Metabolic disorders and nutritional status in autoimmune thyroid diseases. *Advances in Hygiene &*

- Experimental Medicine /Postepy Higieny i Medycyny Doswiadczalnej, 69.
- Kwan, E. Y. W., Lee, A. C. W., Li, A. M. C., Tam, S. C. F., Chan, C. F., Lau, Y. L., & Low, L. C. K. (1995). A cross-sectional study of growth, puberty and endocrine function in patients with thalassaemia major in Hong Kong. *Journal of paediatrics and child health*, 31(2), 83-87.
- Ladenson, P. W., Singer, P. A., Ain, K. B., Bagchi, N., Bigos, S. T., Levy, E. G., ... & Daniels, G. H. (2000). American Thyroid Association guidelines for detection of thyroid dysfunction. *Archives of internal medicine*, 160(11), 1573-1575.
- Leblondel, G., Le Bouil, A., & Allain, P. (1992). of thyroparathyroidectomy and thyroxine replacement on Cu and Zn cellular distribution and on the metallothionein level and induction in rats. *Biological trace element research*, 32(1), 281-288.
- Liabsuetrakul, T. (2011). Is international or Asian criteria-based body mass index associated with maternal anaemia, low birthweight, and preterm Births among Thai population?—an observational study. *Journal of health, population, and nutrition*, 29(3), 218.
- López, G. P., De La Fuente, M. C., Román, M. M., Albarrán, O. G., & Megías, M. C. (2011). Management of hypothyroidism secondary to tyrosine kinase inhibitors: description of treatment in three distinct clinical settings. *Endocrinología y Nutrición (English Edition)*, 2(58), 94-96.
- Mariotti, S., Caturegli, P., Piccolo, P., Barbesino, G., & Pinchera, A. (1990). Antithyroid peroxidase autoantibodies in thyroid diseases. *The Journal of Clinical Endocrinology & Metabolism*, 71(3), 661-669.
- Maxwell, C., & Volpe, S. L. (2007). Effect of zinc supplementation on thyroid hormone function. *Annals of Nutrition and Metabolism*, 51(2), 188-194.
- Moslehi, N., Vafa, M., Rahimi-Foroushani, A., & Golestan, B. (2012). Effects of oral magnesium supplementation on inflammatory markers in middle-aged overweight women. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, 17(7), 607.
- Narayana, S. K., Woods, D. R., & Boos, C. J. (2011). Management of amiodarone-related thyroid problems. *Therapeutic advances in endocrinology and metabolism*, 2(3), 115-126.
- Nazifi, S., Mansourian, M., Nikahval, B., & Razavi, S. M. (2009). The relationship between serum level of thyroid hormones, trace elements and antioxidant enzymes in dromedary camel (*Camelus dromedarius*). *Tropical animal health and production*, 41(1), 129-134.
- Nordyke, R. A., Gilbert, F. I., Miyamoto, L. A., & Fleury, K. A. (1993). The superiority of antimicrobial over antithyroglobulin antibodies for detecting Hashimoto's thyroiditis. *Archives of internal medicine*, 153(7), 862-865.
- O'Kane, S. M., Mulhern, M. S., Pourshahidi, L. K., Strain, J. J., & Yeates, A. J. (2018). Micronutrients, iodine status and concentrations of thyroid hormones: a systematic review. *Nutrition reviews*, 76(6), 418-431.
- OBA, K., & KIMURA, S. (1980). Effects of vitamin A deficiency on thyroid function and serum thyroxine levels in the rat. *Journal of nutritional science and vitaminology*, 26(4), 327-334.
- Oteiza, P. I. (2012). Zinc and the modulation of redox homeostasis. *Free Radical Biology and Medicine*, 53(9), 1748-1759.
- Rabbani, E., Golgiri, F., Janani, L., Moradi, N., Fallah, S., Abiri, B., & Vafa, M. (2021). 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*, 199(11), 4074-4083.
- Rashid, N. F., Abed, B. A., & Abas, T. A. (2010). Relationship between some trace elements, lipid profile and hypothyroidism. *Al Mustansiriyah Journal of Pharmaceutical Sciences*, 8(2), 127-138.
- Rhee, C. M., Bhan, I., Alexander, E. K., & Brunelli, S. M. (2012). Association between iodinated contrast media exposure and incident hyperthyroidism and hypothyroidism. *Archives of internal medicine*, 172(2), 153-159.
- Ruz, M., Codoceo, J., Galgani, J., Muñoz, L., Gras, N., Muzzo, S., ... & Bosco, C. (1999). Single and multiple selenium-zinc-iodine deficiencies affect rat thyroid metabolism and ultrastructure. *The Journal of nutrition*, 129(1), 174-180.
- Santos, R. B., Romaldini, J. H., & Ward, L. S. (2012). A randomized controlled trial to evaluate the effectiveness of 2 regimens of fixed iodine (131I) doses for Graves disease treatment. *Clinical Nuclear Medicine*, 37(3), 241-244.
- Sapin, R., & Schlienger, J. L. (2003, July). Thyroxine (T4) and tri-iodothyronine (T3) determinations: techniques and value in the assessment of thyroid function. In *Annales de biologie clinique* (Vol. 61, No. 4, pp. 411-420).
- Singer, P. A. (1991). Thyroiditis: acute, subacute, and chronic. *Medical Clinics of North America*, 75(1), 61-77.
- Spear, P. A., & Moon, T. W. (1986). Thyroid-vitamin A

- interactions in chicks exposed to 3, 4, 3', 4'-tetrachlorobiphenyl: influence of low dietary vitamin A and iodine. *Environmental research*, 40(1), 188-198.
- Sridevi, D., Dambal, A. A., Sidrah, A. S. C., & Padaki, S. K. (2016). A study of serum magnesium, calcium and phosphorus in hypothyroidism. *Age*, 35(8.85), 35-68.
- Un Nisa, F., Mumtaz, A., Ullah, M. I., Atif, M., & Sami, W. (2013). Determination of serum zinc and magnesium levels in patients with hypothyroidism. *Trace Elements and Electrolytes*, 1-5.
- Wang, K., Wei, H., Zhang, W., Li, Z., Ding, L., Yu, T., & Zhu, M. (2018). Severely low serum magnesium is associated with increased risks of positive anti-thyroglobulin antibody and hypothyroidism: A cross-sectional study. *Scientific reports*, 8(1), 1-9.
- Weetman, A. P., & McGregor, A. M. (1994). Autoimmune thyroid disease: further developments in our understanding. *Endocrine reviews*, 15(6), 788-830.
- Zaichick, V., & Zaichick, S. (2018). Investigation of association between the high risk of female subclinical hypothyroidism and inadequate quantities of twenty intra-thyroidal chemical elements. *Clin Res: Gynecol Obstet*, 1(1), 1-18.
- Zhang, J., Gu, Y., Meng, G., Zhang, Q., Liu, L., Wu, H., & Niu, K. (2021). Association between dietary onion intake and subclinical hypothyroidism in adults: a population-based study from an iodine-replete area. *Endocrine*, 74(3), 616-624.