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Micronutrient-Endocrine Interactions: A Critical Review of the Molecular Mechanisms Underlying Hormonal Regulation – A Case Study from Pakistan, Iran, Azerbaijan and Russia

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Abstract

Essential micronutrients are vital for regulating hormonal balance and supporting the integrity of the endocrine system, which is critical for maintaining optimal human health. By examining facts and analyzing data collected from various primary and secondary sources belong to Pakistan, Iran, Azerbaijan and Russia, this review article interrogates the crucial roles of key micronutrients -- zinc, iodine, selenium, iron and calcium (vitamin D) -- on the endocrine system. Adequate intake of these essential nutrients is important for hormone production. Excess or deficiency of these nutrients can adversely affect health, disturb hormonal balance, and lead to severe diseases. Zinc is crucial for maintaining osteo-muscular integrity, regulating thyroid hormone biosynthesis, and exerting antioxidant properties. Dysregulation of zinc is implicated in the pathogenesis of diabetes mellitus and reproductive dysfunction. Iodine is essential for thyroid hormone synthesis, and its dysregulation can result in hypothyroidism or hyperthyroidism. Additionally, iodine influences cardiovascular health and glucose metabolism. Adequate iodine intake is particularly crucial for pregnant and lactating women to ensure fetal health. In addition to other nutrients, selenium plays a pivotal role in glucose regulation, the production of brain hormones, and metabolism. Its deficiency can lead to metabolic syndrome, obesity, diabetes, and fertility issues. Furthermore, iron overload in thalassemia patients adversely affects hormonal balance. It impacts growth due to abnormal mineralization of bones, disturbs normal sexual development, disrupts thyroid hormone production, and causes diabetes mellitus. Vitamin D and calcium are essential for bone health and parathyroid hormone production. Uncontrolled regulation of these

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hormones can lead to osteoporosis and hyperthyroidism. Moreover, vitamin D is important for heart and muscle contraction, and its disturbance can result in severe disorders such as myocardial infarction and stroke. This review emphasizes the critical role of micronutrient homeostasis in maintaining endocrine function and highlights the underlying mechanisms by which these nutrients modulate hormonal regulation. The article underscores the importance of optimizing micronutrient status to prevent endocrinopathies and promote overall physiological well-being.

Introduction

The endocrine system comprises ductless organs that are highly vascularized, allowing them to synthesize and release hormones into the bloodstream. The secretion of hormones by epithelial cells into the bloodstream enables them to bind to specific receptors on target organs, affecting cellular functions and regulating various physiological processes. The endocrine system is composed of various elements, including the primary endocrine glands (pineal, pituitary, thyroid, parathyroid, and adrenal) and dispersed cells and cell clusters, known as paraganglia, found in the thoracic and abdominal cavities (La Perle & Dintzis, 2017). Endocrine glands release their secretions in the form of hormones that act on target cells through different mechanisms, with hormones utilized by specific cells via autocrine, paracrine, and endocrine actions. The primary role of hormones is to act in various forms to maintain homeostasis in the body (Hackney & Lane, 2015). While endocrine glands play a central role in the endocrine system, other organs, such as the heart, kidneys, bones, and adipose tissue, also perform secondary endocrine functions (Knight et al., 2020; Moser and van der Eerden, 2019).

Micronutrients, as key elements of the body, play essential roles, including immune function, enzyme synthesis, and maintenance of cellular homeostasis. A deficiency in various essential nutrients, especially micronutrients, can adversely affect many physiological actions in the body. Metabolic disorders, compromised immune systems, and altered functions of the endocrine system—particularly the thyroid gland result from micronutrient deficiencies (Godswill et al., 2020; Kopp, 2001). Notably, the human body relies on external sources for these essential nutrients, with almost 30 micronutrients playing a crucial role in maintaining optimal health (Shergill-Bonner, 2017). Indeed, micronutrients significantly influence metabolism. Recent studies have shown that various trace elements are principally involved in enzyme function, participating in enzyme activity within the active site or acting as cofactors. Furthermore, long-term mineral deficiencies due to inadequate intake can have adverse effects on health and may ultimately lead to death (Shenkin, 2006). Micronutrient deficiencies cause negative health effects in the human body. While the deficiency of a single micronutrient is relatively easy to diagnose and treat, recognizing and treating deficiencies of multiple micronutrients simultaneously can be challenging (Shenkin, 2006). Adequate intake of micronutrients, including vitamins and minerals, is essential for maintaining optimal health, particularly for pregnant women, whose nutritional needs directly affect fetal development (Black, 2001).

Zinc-Dependent Hormone Biosynthesis and Regulation

Zinc is considered the 23rd most abundant element found in the Earth's crust (Vallee and Auld, 1989). It has a significant effect on growth and development (Sandstead et al., 1998; Baltaci et al., 2019; Krishnan Krishnamurthy et al., 2023). In adults, the recommended daily intake of zinc is 15 mg; however, this need can be met through diet (Barceloux, 1999). Zinc is naturally present in the body in varying proportions, with a high percentage found in muscle (57%), followed by bone (29%), skin (6%), liver (5%), brain (1.5%), and the lowest concentration in blood plasma (0.1%) (King et al., 2000). Furthermore, zinc enhances the production of specific proteins that promote the activity of osteoblasts and suppress the production of osteoclasts. The absorption of zinc in bones is comparatively higher than in other body tissues, and it also enhances the effect of vitamin D in bone tissue (Salgueiro et al., 2002; Baltaci et al., 2019; Krishnan Krishnamurthy et al., 2023).

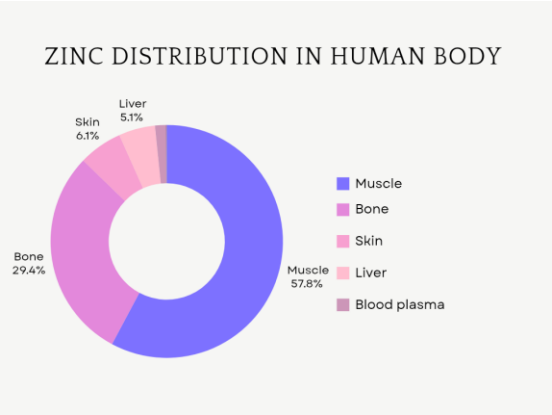

Figure 1: Zinc distribution in the human body. Zinc is distributed throughout the body, with the highest percentages found in muscle and bone. This highlights its essential role in maintaining overall health.

Zinc impacts skeletal cells and the maintenance of bone homeostasis; however, some of its effects have received less attention in research. Bone regeneration is most likely to occur with zinc supplementation, as both bone formation and regeneration are promoted by this mineral. An appropriate dose of zinc is beneficial in this regard; excessive or insufficient concentrations are less effective. Oral ingestion or systemic delivery of zinc is a significant remedial approach to increase zinc levels, particularly for bone regeneration (Agnew & Slesinger, 2020).

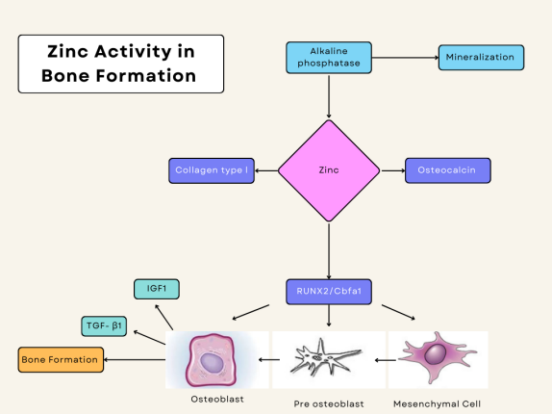

Figure 2: Schematic representation of Zn's role in bone formation. Zn ions (Zn2+) regulate osteoblast activity, promoting bone matrix mineralization and collagen synthesis (Molenda & Kolmas, 2023).

Zinc is considered a trace element beneficial for maintaining normal levels of thyroid hormones, including triiodothyronine (T3), tetraiodothyronine (T4), and thyroid-stimulating hormone (TSH)(Brandao Neto et al., 2006; Kucharzewski et al., 2003). Researchers claim that zinc is involved in antioxidant properties and is an important part of the enzymatic system. It is studied as the most desirable element for hormonal activity, particularly concerning thyroid hormones (Formigari et al., 2007; Catania et al., 2009).

Zinc also functions as an antioxidant in the body. Zinc deficiency causes oxidative stress and contributes to dysfunction of the thyroid gland (Ganapathy and Volpe, 1999). The T3 hormone receptor requires zinc to maintain its biologically active condition (Freake et al., 2001). Additionally, zinc plays a vital role in the production of thyroxin-binding proteins that affect T4 hormone levels in the body (Hartoma et al., 1979). Zinc concentration is affected in thyroid gland diseases, being lower in hypothyroidism and higher in hyperthyroidism (Imamoglu et al., 2005; Baltaci et al., 2019; Krishnan Krishnamurthy et al., 2023). Notably, thyroid disease is considered the most prevalent disease worldwide (Fabrizio, 2003; Garber et al., 2012).

Growth hormones are synthesized and secreted by zinc. A zinc-dependent factor, the insulin-like growth factor (IGF-I), mediates the effects of growth hormone (Brandao-Neto et al., 2006; MacDonald, 2000).

Table 3: Zinc Levels in Diabetes

Concentrations of zinc differ in diabetes; in type II diabetes, plasma or serum zinc levels are lower, whereas in type I diabetes, plasma or serum zinc levels are typically higher (Aguilar et al., 2007; Pedrosa et al., 1999; Baltaci et al., 2019; Krishnan Krishnamurthy et al., 2023).

Diabetes Type	Zinc Levels	Measurement
Type I Diabetes	Typically, higher	Plasma or serum
Type II Diabetes	Lower	Plasma or serum

Therefore, the maintenance of zinc homeostasis in the body is disrupted by hyperglycemia. In diabetic patients, particularly those with hyperglycemia, zinc concentration is drastically lowered due to increased urinary loss (Chausmer, 1998). Similarly, in in vitro tests using isolated liver plasma membranes, it was shown that adding zinc enhanced insulin binding and prevented its breakdown (Arquilla et al., 1978).

Zinc has a significant impact on appetite, including changes in the sense of taste (Jing et al., 2008). Zinc supplementation has been shown to prevent anorexia and weight loss (Birmingham and Gritzner, 2006; Jing et al., 2008). It is postulated that zinc deficiency may lead to leptin resistance (Chen et al., 2000). Zinc also influences testicular tissue (Ozturk et al., 2005) and affects the male reproductive system through gonadotropic hormones (Baltaci et al., 2006). Likewise, zinc plays a crucial role in the reproductive physiology of females (Akhtar et al., 2014; Stallard and Reeves, 1997). It is involved in the pineal gland, which is responsible for the production of melatonin (Johnson, 2001; Fabrizio, 2003; Garber et al., 2012).

Iodine-Dependent Thyroid Hormone Synthesis and Regulation

The Food and Nutrition Board of the National Academy of Sciences of the United States has suggested appropriate dietary intake levels for iodine. The recommended intake is 40 µg per day for infants aged 0 to 6 months, 50 µg for those from 6 months to one year, and 70 µg for children aged one to three years. Recommendations are comparatively higher for adolescents and adults, set at 160 µg per day. Additionally, iodine requirements increase to 220 µg and 290 µg for pregnant and lactating women, respectively (Delange, 1993). However, the WHO indicates that a median urinary iodine level of 100–199 µg/l in a population is regarded as indicative of adequate iodine intake (Lazarus, 2015).

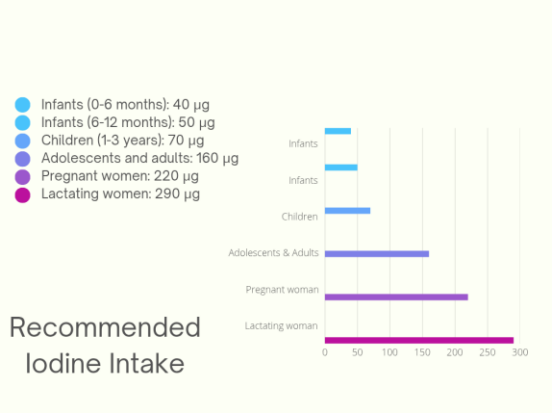

Figure 4: Iodine Recommended Intake Levels. This figure illustrates the recommended dietary intake levels for iodine, as suggested by the Food and Nutrition Board of the National Academy of Sciences.

Iodine, a micronutrient, plays a pivotal role in the biosynthesis of thyroid hormones. When the body is exposed to inappropriate iodine concentrations—whether high or low—it can lead to hyperthyroidism or hypothyroidism, although excess iodine is not easily recognizable(Leung & Braverman, 2014). The primary physiological role of iodine in the human body is to synthesize thyroid hormones in the thyroid gland (World Health Organization, 2005).

Iodine is categorized as a trace element distributed throughout the earth. A sufficient amount of iodine is required to synthesize thyroid hormones, particularly thyroxine (T4) and triiodothyronine (T3). The body may face various clinical disorders if the amount of iodine increases or decreases from an adequate level (Leung et al., 2010). Disproportionation of iodine intake through diet influences blood lipid levels. Excessive intake of iodine may also raise levels of blood glucose and blood pressure, which elevates the

risk of hypertension and diabetes (Liu et al., 2019). Also, autoimmune thyroid disease is caused by excessive intake of iodine (Laurberg et al., 2010).

Studies have indicated that breast milk contains a specific amount of iodine, with reported levels ranging from 5.4 to 2170 µg/L. Maternal iodine intake is not directly affected by several environmental factors. However, the intake of other elements, including selenium and organochlorine pollutants, can impact the maintenance of thyroid hormone homeostasis in breastfed infants (Dorea, 2002). Therefore, the requirement for iodine increases in women during pregnancy and lactation; adequate iodine intake is also necessary even before pregnancy. The prevalence of overweight and obesity is also considered to be influenced by iodine intake. A salt-restricted diet promotes better cardiovascular health, and a plant-based diet is also regarded as healthy (Bath, 2024).

Selenium-Dependent Endocrine Function and Hormone Regulation

Various functions associated with selenium, such as hormonal regulation of glucose and energy metabolism, biosynthesis and action of steroids, neuroendocrine, brain hormones, human development remain contentious and underexplored (Köhrle et al, 2005). In humans, the recommended daily allowance for selenium is between 100 and 200 µg/day. Deficiency of selenium results in selenium-responsive diseases in various animal species, such as muscular dystrophy, exudative diathesis, and hepatitis dietetica (Shamberger, 1981). Selenium, predominantly stored in the thyroid gland, is vital for the formation of various antioxidant enzymes, such as glutathione peroxidase and thioredoxin reductase, as well as the deiodinases that regulate the activation and deactivation of thyroid hormones (Ventura et al., 2017). Furthermore, adequate selenium intake can enhance the production of sialoproteins and thyroid hormones, which, in turn, promote fat metabolism, improve body composition, and reduce the risk of metabolic disorders (Cavedon et al., 2020). However, certain experimental methods and regimens involving selenium compounds may trigger harm, such as oxidative stress or cancer (Peters et al., 2018).

Selenium toxicity can impair endocrine function, resulting in increased thyroid hormone production and a heightened risk of type 2 diabetes (Schomburg, 2020; Yuan et al., 2015). Researchers claim that elevated selenium levels increase the risk of diabetes, with supplements contributing to an 11% increased risk, represented by a risk ratio of 1.11 (95% CI 1.01–1.22). The influence of selenium is compared to placebo in patients, revealing that selenium supplementation carries a higher risk ratio for women than for men (Vinceti et al., 2018).

Conversely, selenium deficiency caused by genetic or environmental factors, such as low dietary intake, can lead to various bodily effects, including an increase in waist circumference, a high BMI, and increased body fat. The author strongly emphasizes that selenium deficiency can be a contributing factor to metabolic syndrome (Ko et al., 2014). Selenium deficiency is implicated in several thyroid gland abnormalities, including increased gland volume, hypothyroidism, autoimmune thyroiditis (Hashimoto's), and the growth of thyroid nodules. Selenium supplementation is recommended to patients significantly affected by Hashimoto’s thyroiditis (Kryczyk-Kozioł et al., 2021). Additionally, Keshan disease, associated with selenium deficiency, has been significantly reduced through a nutrition and food chain selenium supplementation program, which has greatly reduced preventable diseases linked to selenium deficiency (Zhou et al., 2018). Conversely, Deficiency of selenium caused by genetical factors or environmental

factors, for example, low intake in diet can cause various bodily effects such as an increase in waist circumference, a high BMI, and body fat. It is strongly highlighted by the author that deficiency of Se can be a cause of metabolic syndrome (Ko et al., 2014).

Table 5: Selenium Supplementation Benefits

Selenium deficiency is linked to thyroid disorders. Supplementation benefits areas with high prevalence of Hashimoto's thyroiditis (Kryczyk-Kozioł et al., 2021) and prevents Keshan disease (Zhou et al., 2018).

Condition	Benefits
Hashimoto's thyroiditis	Supplementation suggested in highly affected areas
Keshan disease	Successfully prevented in over 90% of already affected local residents

Male infertility can be linked to selenium deficiency, whether due to genetic factors or nutritional deficiencies (Mintziori et al., 2020). A plasma protein called selenoprotein P plays a crucial role in supplying selenium to the testis (Boitani & Puglisi, 2009). Selenium is known to influence both spermatozoa count and motility; disturbances in selenium levels, whether elevated or decreased, negatively impact normal functioning (Hansen & Deguchi, 1996). Additionally, androgens regulate testicular spermatogenesis in males, which is essential for male fertility, but this process can be compromised by selenium deficiency.

Selenoproteins play various roles in female reproduction across many species, including ovarian function, follicular development, and pregnancy. Numerous interventional studies have demonstrated the benefits of selenium in reproductive technologies and in vitro fertilization in humans (Qazi et al., 2018).

Table 6: Selenium and Reproductive Outcomes

Optimal selenium levels (40-70 ng/ml) support reproductive health, increasing pregnancy rates and lowering abortion rates (Bleau et al., 1984; Ingold et al., 2015; Qazi et al., 2018).

Selenium Level (ng/ml)	Reproductive Outcomes
40-70	Increased pregnancy rates Lower abortion rates Optimal for reproductive health Beneficial for normal functioning of the reproductive system
>80	Increased abortion rates Elevated risk of ovarian dysfunction in partners Particularly relevant when both partners follow similar dietary practices Particularly relevant when both partners are exposed to the same environmental factors

Iron-Dependent Endocrine Dysfunction in Thalassemia

This genetic condition, beta thalassemia, disrupts the normal synthesis of beta globin chains, resulting in defective hemoglobin (de Dreuzy et al., 2016). A patient's thalassemic condition is associated with splenectomy, increasing age, severe ineffective erythropoiesis, and low fetal hemoglobin levels (Taher et al., 2009). Thalassemia-associated growth impairment is influenced by several factors, including endocrine disorders, deferoxamine treatment, and hypoxia resulting from anemia; however, studies examining these relationships have yielded conflicting results (Kattamis et al., 1990; Pantelakis, 1994).

In thalassemia patients, iron concentration increases from a moderate level, while there is a decrease in serum cortisol, T4, prolactin, and pancreatic beta cell function percentage. Studies also reveal that serum TSH levels elevate in thalassemia patients. In male thalassemia patients, PCV, Hb, T3, and testosterone levels are higher compared to female patients (Al-Hakeim & Al-Hakany, 2013). In chronic anemic conditions, there is significant iron absorption, resulting in tissue hypoxia, along with compensatory responses such as increased erythropoiesis in the bone marrow and enhanced iron absorption through the intestine. The primary endocrine disorders that thalassemia patients face include growth disorders, sexual development and fertility issues, abnormal bone mineralization, diabetes mellitus, hypothyroidism, and hypoadrenalism (Tiosano & Hochberg, 2001).

Excess iron causes endocrinopathies and growth decline in thalassemia patients. Issues such as low oxygen supply, desferrioxamine toxicity, cardiac overload, nutritional deficiencies, impaired calcium homeostasis, and involvement of the liver and pancreas arise when iron overload occurs in these patients (Soliman et al., 2009; Toumba & Skordis, 2010). Thalassemic patients who undergo transfusions often experience issues such as growth retardation and puberty delay. Initially, with some exceptions, children typically show normal growth during the first decade, but growth failure occurs later on (Low, 1997).

Commonly occurring endocrinopathies in thalassemic patients include hypogonadotropic hypogonadism, diabetes mellitus, and hypothyroidism, even with intensive chelation therapy (Borgna-Pignatti et al., 2004). Approximately 68% of ex-thalassemic patients experience gonadal dysfunction (De Sanctis, 2002). However, if a patient is left untreated, growth disturbances may occur, along with tissue hypoxia and bone marrow disruption (Modell & Berdoukas, 1984).

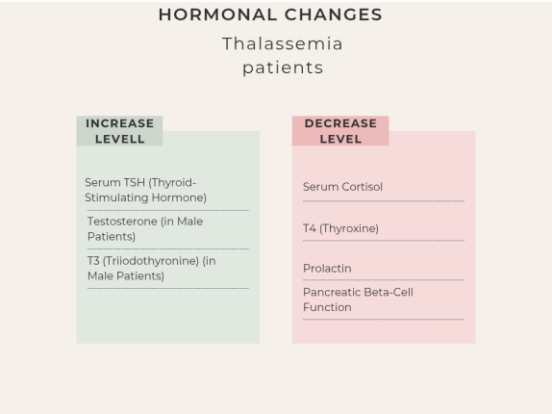

Figure 7: Illustrates the hormonal changes in Thalassemia patients, including decreased levels of serum cortisol, T4, prolactin, and pancreatic beta-cell function, as well as increased levels of serum TSH, testosterone (in male patients), and T3 (in male patients).

Calcium-Dependent Hormone Regulation and Cellular Function

Within the normal range of almost 5%, calcium homeostasis is maintained. Calcium is essential for various intracellular reactions, most importantly in muscle contraction, nerve cell activity, the release of several hormones through exocytosis, and the activation of enzymatic activity. Blood coagulation is primarily controlled by calcium. Moreover, it is important for maintaining cell membrane stability and providing linkages between cells (Greco, 2012). Calcium plays a key role in the maintenance of various cellular activities, such as gene expression, heart and muscle contraction, and motility. It is involved in all significant events that cells undergo, from the initiation of fertilization to the final stages of programmed cell death. The metabolic pathways in which calcium participates provide fuel for the generation of cells (Brini et al., 2013). Furthermore, in humans and various other mammals, calcium serves as an extracellular component in fluids, performing important functions such as maintaining cell membrane integrity and acting as a cofactor in proteins, including adhesion molecules, clotting factors, and secreted enzymes (e.g., trypsin) (Brown, 2013).

Overall, body calcium homeostasis is maintained by vitamin D and its metabolites, which are important components of the endocrine system. Vitamin D's influence on hormonal control helps balance serum calcium levels within a narrow range (Fleet, 2017). However, hypercalcemia is associated with several other diseases, including tuberculosis, lymphoma, disseminated candidiasis, and silicon-induced granuloma (Epstein et al., 1984; Gkonos et al., 1984; Breslau et al., 1984; Rosenthal et al., 1985; Kantarjian et al., 1983; Kozeny et al., 1984). Calcium concentrations in extracellular fluid can vary when hormonal levels are disturbed. Low or high production of hormones, or tumors related to parathyroid hormone, can disrupt calcium concentrations (Mundy & Guise, 1999). Disturbances in serum 1,25(OH)2D levels can also lead to issues; excess levels can cause hypercalcemia (Barbour et al., 1981). The renal synthesis of 1,25(OH)2D is regulated by parathyroid hormone. In cases of hyperparathyroidism, serum 1,25(OH)2D levels increase, while in hypoparathyroidism, these levels decrease (Haussler et al., 1976; Lambert et al., 1980). Both parathyroid hormone and 1,25(OH)2D are responsible for changes in calcium absorption levels in the body, corresponding to variations in dietary calcium intake (Gallagher et al., 1979; Norman et al., 1981).

Table 8: Comparison of Hormonal and Calcium Levels in Hyperparathyroidism and Hypoparathyroidism.

Condition	Serum 1,25(OH)2D Levels	Parathyroid Hormone (PTH) Levels	Calcium Levels
Hyperparathyroidism	Increase	Elevated	Hypercalcemia
Hypoparathyroidism	Decrease	Low	Hypocalcemia

Alterations in the vitamin D endocrine system have been particularly recognized in obese men (Cohn et al., 1977). Obesity is considered an important condition in which vitamin D levels are disrupted, affecting the endocrine system. This has a secondary effect on parathyroid hormone production, which enhances tubular reabsorption of calcium and increases renal production of 1,25(OH)2D (Dalen et al., 1975).

Elevated calcium levels can pose health risks, including the formation of kidney stones and an increased susceptibility to cardiovascular events like heart attacks and strokes (Pu et al., 2016). The body synthesizes vitamin D through skin exposure to UV radiation or obtains it through diet. The vitamin then undergoes a series of hydroxylation reactions in the liver and kidneys, transforming 25(OH)D into 1,25(OH)2D (Carmeliet et al., 2003). In postmenopausal women, high concentrations of calcium excreted from the body have been analyzed, suggesting that this may be due to an increase in plasma bicarbonate and anion gap (Nordin, 1990).

Table 9: Micronutrients, Deficiencies and associated Disorders.

Micronutrients	Deficiency Effects	Associated Disorders
Zinc	*Impaired bone formation* *Hypothyroidism, goiter* *Impaired glucose metabolism* *Impaired growth, development* *Impaired fertility, hypogonadism* *Anorexia, weight loss*	**Osteoporosis** **Hypothyroidism, goiter** **Type II diabetes** **Growth hormone deficiency** **Hypogonadism** **Anorexia nervosa**
Iodine	*Hypothyroidism, goiter* *Autoimmune thyroid disease* *Adverse effects on lactation and reproductive functions*	**Hypothyroidism, goiter** **Autoimmune thyroid disease** **Reproductive disorders**
Selenium	*Impaired thyroid function* *Increased risk of type 2 diabetes* *Metabolic syndrome* *Male infertility* *Ovarian dysfunction* *Keshan disease*	**Hypothyroidism, Hashimoto's thyroiditis** **Type 2 diabetes** **Metabolic syndrome** **Male infertility** **Ovarian dysfunction** **Keshan disease**
Iron	*Growth disorders* *Sexual development and fertility issues* *Abnormal bone mineralization* *Diabetes mellitus* *Hypothyroidism* *Hypoadrenalism*	**Growth hormone deficiency** **Hypogonadism** **Osteoporosis** **Type II diabetes** **Hypothyroidism** **Adrenal insufficiency**
Calcium	*Hypocalcemia*	**Osteoporosis, tetany, muscle cramps** **Hyperparathyroidism, hypoparathyroidism**

	Disturbances in serum 1,25(OH)2D levels *Obesity-related disorders*	**Vitamin D deficiency, parathyroid hormone imbalance**

Conclusion

The complicated connection between the endocrine system and micronutrients emphasizes the importance of maintaining sufficient and balanced nutrient levels for hormonal well-being. The production, regulation, and function of several hormones depend on the elements zinc, iodine, selenium, iron, and calcium (vitamin D). These micronutrients significantly impact endocrine health, influencing everything from bone health and reproductive functions to insulin sensitivity and thyroid function.

Many hormonal pathways, including those involved in development and reproduction, rely on zinc. Iodine, which is crucial for thyroid function, can lead to thyroid diseases if present in excess or deficiency. The role of selenium highlights the need for a careful balance, as it supports thyroid function and possesses antioxidant properties. Iron imbalances, whether too little or too much, can lead to significant endocrine disruptions, such as anemia and thalassemia. Additionally, an imbalance of calcium and vitamin D is associated with conditions like osteoporosis and hyperparathyroidism, as both nutrients are essential for maintaining bone health and normal parathyroid function. Adequate intake of these micronutrients is vital for the health of endocrine glands and the preservation of hormonal balance, but there are serious risks associated with both excesses and deficiencies.

This review focuses on the importance of maintaining optimal levels of these micronutrients to support endocrine health and prevent related illnesses. A balanced intake through diet and, if necessary, supplements can significantly impact overall health and hormonal wellness. Future research and public health policies should continue to center on this crucial topic to better understand the mechanisms behind micronutrient functions in endocrine health and improve preventive and therapeutic approaches.

References

La Perle, K. M. D., & Dintzis, S. M. (2017). Endocrine system. In Elsevier eBooks (pp. 251–273). https://doi.org/10.1016/b978-0-12-802900-8.00015-4

Hackney, A. C., & Lane, A. R. (2015). Exercise and the regulation of endocrine hormones. Progress in Molecular Biology and Translational Science, 293–311. https://doi.org/10.1016/bs.pmbts.2015.07.001

Godswill, A. G., Somtochukwu, I. V., Ikechukwu, A. O., & Kate, E. C. (2020). Health Benefits of Micronutrients (Vitamins and Minerals) and their Associated Deficiency Diseases: A Systematic Review. International Journal of Food Sciences, 3(1), 1–32. https://doi.org/10.47604/ijf.1024

Kopp, P. (2001). Human Genome and Diseases: Review¶The TSH receptor and its role in thyroid disease. Cellular and Molecular Life Sciences, 58(9), 1301–1322. https://doi.org/10.1007/pl00000941

Shergill-Bonner, R. (2017). Micronutrients. Paediatrics and Child Health, 27(8), 357–362. https://doi.org/10.1016/j.paed.2017.04.002

Shenkin, A. (2006). The key role of micronutrients☆. Clinical Nutrition, 25(1), 1–13. https://doi.org/10.1016/j.clnu.2005.11.006

Shenkin, A. (2006). Micronutrients in health and disease. Postgraduate Medical Journal,82(971),559–567.https://doi.org/10.1136/pgmj.2006.047670

Black, R. E. (2001). Micronutrients in pregnancy. British Journal of Nutrition, 85(S2), S193–S197. https://doi.org/10.1079/bjn2000314

Baltaci, A. K., Mogulkoc, R., & Baltaci, S. B. (2019). The role of zinc in the endocrine system. https://hdl.handle.net/20.500.12395/38324

Krishnamurthy, H. K., Reddy, S., Jayaraman, V., Krishna, K., Rajasekaran, K. E., Wang, T., Bei, K., & Rajasekaran, J. J. (2023). Association of micronutrients and prevalence of antibodies in hyperthyroidism. In IntechOpen eBooks. https://doi.org/10.5772/intechopen.109375

Barceloux D. G. (1999). Zinc. Journal of toxicology. Clinical toxicology, 37(2), 279–292. https://doi.org/10.1081/clt-100102426

King, J. C., Shames, D. M., & Woodhouse, L. R. (2000). Zinc homeostasis in humans. Journal of Nutrition, 130(5), 1360S-1366S. https://doi.org/10.1093/jn/130.5.1360s

Agnew, U. M., & Slesinger, T. L. (2023). Zinc toxicity. In StatPearls. StatPearls Publishing. PMID: 32119435

Brandão-Neto, J., Saturnino, A. C. R. D., Leite, L. D., De Medeiros Rocha, É. D., Marcos, C. M. P., Da Silva, C. a. B., Marchini, J. S., De Rezende, A. A., Almeida, M. D. G., & Da Cunha Medeiros, A. (2006). Lack of acute zinc effect on thyrotropin-releasing hormone–stimulated thyroid-stimulating hormone secretion during oral zinc tolerance test in healthy men. Nutrition Research, 26(10), 493–496. https://doi.org/10.1016/j.nutres.2006.08.010

Kucharzewski, M., Braziewicz, J., Majewska, U., & Gózdz, S. (2003). Copper, Zinc, and Selenium in Whole Blood and Thyroid Tissue of People with Various Thyroid Diseases. Biological Trace Element Research, 93(1–3), 9–18. https://doi.org/10.1385/bter:93:1-3:9

Molenda, M., & Kolmas, J. (2023). The role of zinc in bone tissue health and regeneration—a review. Biological Trace Element Research, 201(12), 5640–5651. https://doi.org/10.1007/s12011-023-03631-1

Formigari, A., Irato, P., & Santon, A. (2007). Zinc, antioxidant systems and metallothionein in metal mediated-apoptosis: Biochemical and cytochemical aspects. Comparative Biochemistry and Physiology Part C Toxicology & Pharmacology, 146(4), 443–459. https://doi.org/10.1016/j.cbpc.2007.07.010

Catania, A. S., Barros, C. R., & Ferreira, S. R. (2009). Vitaminas e minerais com propriedades antioxidantes e risco cardiometabólico: controvérsias e perspectivas [Vitamins and minerals with

antioxidant properties and cardiometabolic risk: controversies and perspectives]. Arquivos brasileiros de endocrinologia e metabologia, 53(5), 550–559. https://doi.org/10.1590/s0004-27302009000500008

Monaco, F. (2003). Classification of Thyroid Diseases: Suggestions for a revision. The Journal of Clinical Endocrinology & Metabolism, 88(4), 1428–1432. https://doi.org/10.1210/jc.2002-021260

Garber, J. R., Cobin, R. H., Gharib, H., Hennessey, J. V., Klein, I., Mechanick, J. I., Pessah-Pollack, R., Singer, P. A., & Woeber, K. A. (2012). Clinical Practice Guidelines for Hypothyroidism in Adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocrine Practice, 18(6), 988–1028. https://doi.org/10.4158/ep12280.gl

Chausmer, A. B. (1998). Zinc, insulin and diabetes. Journal of the American College of Nutrition, 17(2), 109–115. https://doi.org/10.1080/07315724.1998.10718735

Arquilla, E. R., Packer, S., Tarmas, W., & Miyamoto, S. (1978). The effect of zinc on insulin metabolism. Endocrinology, 103(4), 1440–1449. https://doi.org/10.1210/endo-103-4-1440

Delange, F. (1993). Requirements of iodine in humans. In Springer eBooks (pp. 5–15). https://doi.org/10.1007/978-1-4899-1245-9_1

Lazarus, J. H. (2015). The importance of iodine in public health. Environmental Geochemistry and Health, 37(4), 605–618. https://doi.org/10.1007/s10653-015-9681-4

Leung, A. M., & Braverman, L. E. (2013). Consequences of excess iodine. Nature Reviews Endocrinology, 10(3), 136–142. https://doi.org/10.1038/nrendo.2013.251

World Health Organization. (2005). Vitamin and mineral requirements in human nutrition (2nd ed.). World Health Organization.

Leung, A., Pearce, E. N., & Braverman, L. E. (2010). Role of iodine in thyroid physiology. Expert Review of Endocrinology & Metabolism, 5(4), 593–602. https://doi.org/10.1586/eem.10.40

Liu, J., Liu, L., Jia, Q., Zhang, X., Jin, X., & Shen, H. (2019). Effects of excessive iodine intake on blood glucose, blood pressure, and blood lipids in adults. Biological Trace Element Research, 192(2), 136–144. https://doi.org/10.1007/s12011-019-01668-9

Laurberg, P., Cerqueira, C., Ovesen, L., Rasmussen, L. B., Perrild, H., Andersen, S., Pedersen, I. B., & Carlé, A. (2010). Iodine intake as a determinant of thyroid disorders in populations. Best Practice & Research Clinical Endocrinology & Metabolism, 24(1), 13–27. https://doi.org/10.1016/j.beem.2009.08.013

Dorea, J. G. (2002). Iodine nutrition and breast feeding. Journal of Trace Elements in Medicine and Biology, 16(4), 207–220. https://doi.org/10.1016/s0946-672x(02)80047-5

Bath, S. C. (2024). Thyroid function and iodine intake: global recommendations and relevant dietary trends. Nature Reviews Endocrinology, 20(8), 474–486. https://doi.org/10.1038/s41574-024-00983-z

KöHrle, J., Jakob, F., Contempre, B., & Dumont, J. E. (2005). Selenium, the thyroid, and the endocrine system. Endocrine Reviews, 26(7), 944–984. https://doi.org/10.1210/er.2001-0034

Ventura, M., Melo, M., & Carrilho, F. (2017). Selenium and thyroid disease: From pathophysiology to treatment. International Journal of Endocrinology, 2017, 1–9. https://doi.org/10.1155/2017/1297658

Cavedon, E., Manso, J., Negro, I., Censi, S., Serra, R., Busetto, L., Vettor, R., Plebani, M., Pezzani, R., Nacamulli, D., & Mian, C. (2020). Selenium Supplementation, Body Mass Composition, and Leptin Levels in Patients with Obesity on a Balanced Mildly Hypocaloric Diet: A Pilot Study. International Journal of Endocrinology, 2020, 1–7. https://doi.org/10.1155/2020/4802739

Peters, K. M., Carlson, B. A., Gladyshev, V. N., & Tsuji, P. A. (2018). Selenoproteins in colon cancer. Free Radical Biology and Medicine, 127, 14–25. https://doi.org/10.1016/j.freeradbiomed.2018.05.075

Schomburg, L. (2019). The other view: the trace element selenium as a micronutrient in thyroid disease, diabetes, and beyond. HORMONES, 19(1), 15–24. https://doi.org/10.1007/s42000-019-00150-4

Yuan, Z., Xu, X., Ye, H., Jin, L., Zhang, X., & Zhu, Y. (2015). High levels of plasma selenium are associated with metabolic syndrome and elevated fasting plasma glucose in a Chinese population: A case-control study. Journal of Trace Elements in Medicine and Biology, 32, 189–194. https://doi.org/10.1016/j.jtemb.2015.07.009

Vinceti, M., Filippini, T., & Rothman, K. J. (2018). Selenium exposure and the risk of type 2 diabetes: a systematic review and meta-analysis. European Journal of Epidemiology, 33(9), 789–810. https://doi.org/10.1007/s10654-018-0422-8

Bj, K., Sm, K., Kh, P., Hs, P., & Cs, M. (2014). Levels of circulating selenoprotein P, fibroblast growth factor (FGF) 21 and FGF23 in relation to the metabolic syndrome in young children. International Journal of Obesity, 38(12), 1497–1502. https://doi.org/10.1038/ijo.2014.45

Kryczyk-Kozioł, J., Zagrodzki, P., Prochownik, E., Błażewska-Gruszczyk, A., Słowiaczek, M., Sun, Q., Schomburg, L., Ochab, E., & Bartyzel, M. (2021). Positive effects of selenium supplementation in women with newly diagnosed Hashimoto's thyroiditis in an area with low selenium status. International Journal of Clinical Practice, 75(9). https://doi.org/10.1111/ijcp.14484

Zhou, H., Wang, T., Li, Q., & Li, D. (2018). Prevention of Keshan Disease by Selenium Supplementation: a Systematic Review and Meta-analysis. Biological Trace Element Research, 186(1), 98–105. https://doi.org/10.1007/s12011-018-1302-5

Mintziori, G., Mousiolis, A., Duntas, L. H., & Goulis, D. G. (2019). Evidence for a manifold role of selenium in infertility. HORMONES, 19(1), 55–59. https://doi.org/10.1007/s42000-019-00140-6

Boitani, C., & Puglisi, R. (2009). Selenium, a key element in spermatogenesis and male fertility. Advances in Experimental Medicine and Biology, 65–73. https://doi.org/10.1007/978-0-387-09597-4_4

Hansen, J. C., & Deguchi, Y. (1996). Selenium and Fertility in Animals and Man–A Review. Acta Veterinaria Scandinavica, 37(1), 19–30. https://doi.org/10.1186/bf03548116

Bleau, G., Lemarbre, J., Faucher, G., Roberts, K. D., & Chapdelaine, A. (1984). Semen selenium and human fertility. Fertility and Sterility, 42(6), 890–894. https://doi.org/10.1016/s0015-0282(16)48261-0

Ingold, I., Aichler, M., Yefremova, E., Roveri, A., Buday, K., Doll, S., Tasdemir, A., Hoffard, N., Wurst, W., Walch, A., Ursini, F., Angeli, J. P. F., & Conrad, M. (2015). Expression of a catalytically inactive mutant form of glutathione peroxidase 4 (GPX4) confers a dominant-negative effect in male fertility. Journal of Biological Chemistry, 290(23), 14668–14678. https://doi.org/10.1074/jbc.m115.656363

Qazi, I. H., Angel, C., Yang, H., Pan, B., Zoidis, E., Zeng, C., Han, H., & Zhou, G. (2018). Selenium, selenoproteins, and Female Reproduction: A review. Molecules, 23(12), 3053. https://doi.org/10.3390/molecules23123053

De Dreuzy, E., Bhukhai, K., Leboulch, P., & Payen, E. (2016). Current and future alternative therapies for beta-thalassemia major. Biomedical Journal, 39(1), 24–38. https://doi.org/10.1016/j.bj.2015.10.001

Taher, A. T., Musallam, K. M., Karimi, M., El-Beshlawy, A., Belhoul, K., Daar, S., Saned, M., El-Chafic, A., Fasulo, M. R., & Cappellini, M. D. (2009). Overview on practices in thalassemia intermedia management aiming for lowering complication rates across a region of endemicity: the OPTIMAL CARE study. Blood, 115(10), 1886–1892. https://doi.org/10.1182/blood-2009-09-243154

Kattamis, C., Liakopoulou, T., & Kattamis, A. (1990). Growth and Development in Children with Thalassaemia Major. Acta Paediatrica, 79(s366), 111–117. https://doi.org/10.1111/j.1651-2227.1990.tb11611.x

Pantelakis, S. (1994). Growth patterns in patients with thalassaemia major. Acta Paediatrica, 83(s406), 109–110. https://doi.org/10.1111/j.1651-2227.1994.tb13437.x

Al-Hakeim, H. K. a. H., & Al-Hakany, M. F. M. (2013, December 2). The effect of iron overload on the function of some endocrine glands in B-Thalassemia major patients. https://journal.uokufa.edu.iq/index.php/ajb/article/view/7776

Tiosano, D., & Hochberg, Z. (2001). Endocrine complications of thalassemia. Journal of Endocrinological Investigation, 24(9), 716–723. https://doi.org/10.1007/bf03343916

Soliman, A. T., Khalafallah, H., & Ashour, R. (2009). Growth and Factors Affecting it in Thalassemia Major. Hemoglobin, 33(sup1), S116–S126. https://doi.org/10.3109/03630260903347781

Toumba, M., & Skordis, N. (2010). Osteoporosis Syndrome in Thalassaemia Major: An Overview. Journal of Osteoporosis, 2010, 1–7. https://doi.org/10.4061/2010/537673

Low, L. C. (1997). Growth, puberty and endocrine function in Beta-Thalassaemia major. Journal of Pediatric Endocrinology and Metabolism, 10(2). https://doi.org/10.1515/jpem.1997.10.2.175

Borgna-Pignatti, C., Rugolotto, S., De Stefano, P., Zhao, H., Cappellini, M., Del Vecchio, G., Romeo, M., Forni, G., Gamberini, Ghilardi, R., Piga, A., & Cnaan, A. (2004, January 1). Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. https://www.haematologica.org/haematologica/article/view/3248

De Sanctis, V. (2002). Growth and Puberty and its management in thalassaemia. Hormone Research in Paediatrics, 58(Suppl. 1), 72–79. https://doi.org/10.1159/000064766

Rebulla, P., & Modell, B. (1991). Transfusion requirements and effects in patients with thalassaemia major. The Lancet, 337(8736), 277–280. https://doi.org/10.1016/0140-6736(91)90881-o

Greco, D. S. (2012). Endocrine causes of calcium disorders. Topics in Companion Animal Medicine, 27(4), 150–155. https://doi.org/10.1053/j.tcam.2012.11.001

Brini, M., Calì, T., Ottolini, D., & Carafoli, E. (2012). Intracellular calcium homeostasis and signaling. Metal Ions in Life Sciences, 119–168. https://doi.org/10.1007/978-94-007-5561-1_5

Brown, E. M. (2013). Role of the calcium-sensing receptor in extracellular calcium homeostasis. Best Practice & Research Clinical Endocrinology & Metabolism, 27(3), 333–343. https://doi.org/10.1016/j.beem.2013.02.006

Fleet, J. C. (2017). The role of vitamin D in the endocrinology controlling calcium homeostasis. Molecular and Cellular Endocrinology, 453, 36–45. https://doi.org/10.1016/j.mce.2017.04.008

Barré, P. E., Gascon-Barré, M., Meakins, J. L., & Goltzman, D. (1987). Hydroxychloroquine treatment of hypercalcemia in a patient with sarcoidosis undergoing hemodialysis. The American Journal of Medicine, 82(6), 1259–1262. https://doi.org/10.1016/0002-9343(87)90237-3

Epstein, S., Stern, P. H., Bell, N. H., Dowdeswell, I., & Turner, R. T. (1984). Evidence for abnormal regulation of circulating 1α,25-dihydroxyvitamin D in patients with pulmonary tuberculosis and normal calcium metabolism. Calcified Tissue International, 36(1), 541–544. https://doi.org/10.1007/bf02405362

Gkonos, P. J., London, R., & Hendler, E. D. (1984). Hypercalcemia and Elevated 1,25-Dihydroxyvitamin D Levels in a Patient with End-Stage Renal Disease and Active Tuberculosis. New England Journal of Medicine, 311(26), 1683–1685. https://doi.org/10.1056/nejm198412273112607

Breslau, N. A. (1984). Hypercalcemia Associated with Increased Serum Calcitriol Levels in Three Patients with Lymphoma. Annals of Internal Medicine, 100(1), 1. https://doi.org/10.7326/0003-4819-100-1-1

Rosenthal, N., Insogna, K. L., Godsall, J. W., Gac, A., Smaldone, L., Waldron, J. A., & Stewart, A. F. (1985). Elevations in Circulating 1,25-Dihydroxyvitamin D in Three Patients with Lymphoma-Associated Hypercalcemia*. The Journal of Clinical Endocrinology & Metabolism, 60(1), 29–33. https://doi.org/10.1210/jcem-60-1-29

Kantarjian, H. M., Saad, M. F., Estey, E. H., Sellin, R. V., & Samaan, N. A. (1983). Hypercalcemia in disseminated candidiasis. The American Journal of Medicine, 74(4), 721–724. https://doi.org/10.1016/0002-9343(83)91033-1

Kozeny, G. A., Barbato, A. L., Bansal, V. K., Vertuno, L. L., & Hano, J. E. (1984). Hypercalcemia Associated with Silicone-Induced Granulomas. New England Journal of Medicine, 311(17), 1103–1105. https://doi.org/10.1056/nejm198410253111707

Mundy, G. R., & Guise, T. A. (1999). Hormonal control of calcium homeostasis. Clinical Chemistry, 45(8), 1347–1352. https://doi.org/10.1093/clinchem/45.8.1347

Bell, N. H., Epstein, S., Greene, A., Shary, J., Oexmann, M. J., & Shaw, S. (1985). Evidence for alteration of the vitamin D-endocrine system in obese subjects. Journal of Clinical Investigation, 76(1), 370–373. https://doi.org/10.1172/jci111971

Lambert, P. W., Hollis, B. W., Bell, N. H., & Epstein, S. (1980). Demonstration of a lack of change in serum 1 alpha,25-dihydroxyvitamin D in response to parathyroid extract in pseudohypoparathyroidism. Journal of Clinical Investigation, 66(4), 782–791. https://doi.org/10.1172/jci109916

Gallagher, J. C., Riggs, B. L., Eisman, J., Hamstra, A., Arnaud, S. B., & Deluca, H. F. (1979). Intestinal calcium absorption and serum vitamin D metabolites in normal subjects and osteoporotic patients. Journal of Clinical Investigation, 64(3), 729–736. https://doi.org/10.1172/jci109516

Norman, D. A., Fordtran, J. S., Brinkley, L. J., Zerwekh, J. E., Nicar, M. J., Strowig, S. M., & Pak, C. Y. (1981). Jejunal and ileal adaptation to alterations in dietary calcium: changes in calcium and magnesium absorption and pathogenetic role of parathyroid hormone and 1,25-dihydroxyvitamin D. Journal of Clinical Investigation, 67(6), 1599–1603. https://doi.org/10.1172/jci110194

Cohn, S., Abesamis, C., Yasumura, S., Aloia, J., Zanzi, I., & Ellis, K. (1977). Comparative skeletal mass and radial bone mineral content in black and white women. Metabolism, 26(2), 171–178. https://doi.org/10.1016/0026-0495(77)90052-x

Dalén, N., Hallberg, D., & Lamke, B. (1975). BONE MASS IN OBESE SUBJECTS. Acta Medica Scandinavica, 197(1–6), 353–355. https://doi.org/10.1111/j.0954-6820.1975.tb04933.x

Pu, F., Chen, N., & Xue, S. (2016). Calcium intake, calcium homeostasis and health. Food Science and Human Wellness, 5(1), 8–16. https://doi.org/10.1016/j.fshw.2016.01.001

Carmeliet, G., Van Cromphaut, S., Daci, E., Maes, C., & Bouillon, R. (2003). Disorders of calcium homeostasis. Best Practice & Research Clinical Endocrinology & Metabolism, 17(4), 529–546. https://doi.org/10.1016/j.beem.2003.08.001

Nordin, B. (1990). Calcium homeostasis. Clinical Biochemistry, 23(1), 3–10. https://doi.org/10.1016/0009-9120(90)90309-i