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The impact of physical activity and diet in the treatment of hypothyroidism: A systematic review

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Abstract

Introduction and Objective: Thyroid diseases constitute a significant health challenge of the 21st century. Due to the growing awareness of the accompanying symptoms and the impact of the proper functioning of the thyroid gland on the overall condition of the body, patients show increasing interest in therapeutic methods. The main aim of the article is to present the impact of physical activity and proper diet on the management of patients with hypothyroidism.

Review and Methods: Review and summary of studies and meta-analysis of studies available in open-source format on Google Scholar, Web of Science and PubMed.

Abbreviated Description of the State of Knowledge: Hypothyroidism is a clinical condition characterized by the insufficient production of thyroid hormones by the thyroid gland. This hormonal deficiency leads to a generalized decrease in metabolic processes. Clinically, hypothyroidism is diagnosed based on elevated serum levels of thyroid-stimulating hormone (TSH) and decreased levels of free thyroxine (T4). Prevalent symptoms include fatigue, constipation, weight gain, cold intolerance, depression and dry skin. Effective management typically involves hormone replacement therapy with synthetic thyroxine.

Summary: Hypothyroidism is a complex disease influenced by many factors. A multidisciplinary approach is recommended in its treatment, including pharmacological treatment, diet and appropriately selected physical activity. Early diagnosis and treatment are essential to improve the physical and mental condition of patients.

Keywords: hypothyroidism, diet, physical activity

Introduction

Hypothyroidism is a common condition caused by deficiency of thyroid hormones. The production of thyroxine decreases and as a result triiodothyronine activity in cells is insufficient. Consequently, metabolic processes slow down. Also fibronectin and hydrophilic glycosaminoglycans in the subcutaneous tissue, muscles, and other tissues accumulate causing interstitial oedema. Hypothyroidism is classified as primary, central or peripheral. Primary if the pathology is located in the thyroid gland, secondary in pituitary gland or hypothalamus or peripheral in peripheral tissue. The most common form is acquired primary hypothyroidism. Nowadays in well developed countries it is usually caused by chronic autoimmune thyroiditis (Hashimoto thyroiditis). Another prevalent reason is severe iodine deficiency. Hashimoto thyroiditis is an autoimmune disease. Autoimmune diseases are caused by dysregulation of immunologic response. Immune system starts identifying its own tissues as foreign antigen and launches an immune response that damages those tissues. In Hashimoto disease thyroid tissue is attacked by antibodies. It leads to progressive fibrosis and hypothyroidism.

Regardless of the underlying cause of the disease, patients can develop a variety of symptoms. Most of them are non-specific and prevalent in the population. That is why we need to check levels of TSH and fT4 in blood to confirm diagnosis. In primary hypothyroidism TSH raises and fT4 is decreased. At the beginning patients usually suffer from constipation, fatigue, dry skin, and weight gain. Then other symptoms start to appear: cold intolerance, decreased sweating, nerve deafness, peripheral neuropathy, decreased energy, depression, dementia, memory loss, muscle cramps, joint pain, hair loss, apnea, menorrhagia, and voice hoarseness resulting from goiter enlargement. The disease also has cardiovascular consequences such as increased peripheral vascular resistance, decreased cardiac output and bradycardia. Reduced pulmonary and cardiac reserves, along with loss of muscle strength, lead to fatigue, exertional dyspnea, and exercise intolerance. In addition some patients accumulate fluid in cavities like pleural and pericardial cavities. Hypothyroidism can even be fatal. Myxoedema coma is rare but leading to death, which develops when adaptive mechanisms fail to maintain homeostasis. As we can see thyroid hormones are crucial to proper function of the organism [1].

Materials and methods

A comprehensive review of the scientific literature on hypothyroidism and the role of diet and physical activity in its pathogenesis was conducted. A systematic search was performed using the PubMed, Google Scholar, and Web of Science databases. In order to ensure the inclusion of the most current data, the articles were selected based on their publication date, with a focus on those published within the last decade.

The inclusion criteria encompassed articles written in both English and Polish, including original research studies, meta-analyses, clinical trials, and review articles. Articles written in languages other than English, case reports, commentaries, and letters were excluded from the review. A combination of Medical Subject Headings (MeSH) terms and key phrases related to the aforementioned topics was used to search the literature, including "hypothyroidism", "diet", "physical activity", "epidemiology", "diagnosis" and "treatment." The articles were then evaluated to determine their relevance and suitability for inclusion in this study.

The review work also drew on knowledge from specialist books on related topics.

Review

Hypothyroidism and comorbidity

Hypothyroidism is known to lead to weight gain, which can be attributed to several factors. One of them is accumulation of fluids and mucopolysaccharides in subcutaneous tissue causing oedema. On the other hand, fatigue and decreased endurance lead to reduced physical activity. Basal metabolism and thermogenesis are reduced, too. It seems that resting energy expenditure in obese women with hypothyroidism even when levothyroxine therapy is appropriate is decreased in comparison to obese women with proper thyroid function [2]. This leads to being overweight or obesity. Most studies show positive correlation between BMI and TSH level, but it is not so clear when we talk about fT4 level. If we consider only studies with over 1000 participants negative correlation can be observed [3]. Additionally, genetic susceptibility to hypothyroidism is correlated with a higher risk of elevated BMI [4]. Meta-analysis of 22 studies revealed a positive correlation between obesity and an increased risk of hypothyroidism. Additionally, the research indicated an association between obesity and elevated levels of thyroid peroxidase antibodies (TPOAb), which play a fundamental role in the pathogenesis of Hashimoto's thyroiditis. This relationship may be attributed to the fact that obesity induces chronic inflammation through the production of proinflammatory cytokines by adipose tissue. Moreover, leptin, a hormone produced by adipocytes, is another factor contributing to inflammation [5].

Type 2 diabetes is more common in people with hypothyroidism [6]. Thyroid hormones also regulate insulin production and glucose absorption in skeletal muscles, adipose tissue and liver. Patients with hypothyroidism present reduced glucose transport and utilization. This results in insulin resistance which is the underlying cause of type 2 diabetes and initiates Bcell dysfunction. Additionally, liver gluconeogenesis and glycogenolysis decrease [7].

A different mechanism is the basis of type 1 diabetes and Hashimoto disease. Both diseases are prevalent autoimmune disorders. Up to 25% of patients with type 1 diabetes produce autoantibodies predisposing to thyroid disease [8] and more than 10% develop overt Hashimoto's thyroiditis [9]. Genetic factors are also involved in pathogenesis [10] and many genes underlying both disorders have been identified [11]. Studies show that a family of individuals with one disease is more likely to suffer from the other disorder [12-14].

Patients with hypothyroidism also have problems with abnormal lipid profiles. Hepatic expression of LDL receptors decreases. As a result, the LDL level increases. Impaired thyroid function is expected to raise serum total cholesterol, LDL-C, and triglycerides, while decreasing HDL levels. Treatment with levothyroxine is helpful in normalizing those changes [15].

Physical activity in hypothyroidism - benefits and obstacles

There is no consensus among researchers on how physical exercise activity impacts the levels of thyroid hormones and studies are inconclusive. The study with 2740 healthy participants did not reveal any changes in TSH and fT4 after training [16]. On the other hand there are studies that show an association between daily physical activity and changes in thyroid hormone levels: more active individuals had a better thyroid function [17].

Despite the fact that evidence generally does not seem to support the notion that physical activity has a direct and significant impact on thyroid function, such as, decreasing TSH and increasing fT4 levels, it can improve physical and mental health for example by lowering body fat percentage, systolic blood pressure, better sit and reach test results [18]. Regardless of the barriers that may occur as a result of hypothyroidism, physical activity should still be performed, as well as exercising. Both aerobic and resistance training appeared to be safe [19]. Despite numerous benefits of physical activity, patients with hypothyroidism often limit their daily activities and exercise. Factors such as fatigue, muscle weakness, reduced pulmonary and cardiac reserves, and depression make it challenging for them to adhere to physical activity recommendations. According to studies individuals with hypothyroidism are highly likely to fall into a vicious cycle of poor physical condition due to physical constraints. Even if treated with levothyroxine, some patients experience impaired quality of life. Complaints are more severe in patients with autoimmune thyroiditis [20].

Thyroid hormones also affect the cardiovascular system. In hypothyroidism relaxation of vascular smooth muscle is impaired and accessibility of nitric oxide is decreased which leads to lower cardiac output and results in arterial stiffness. Peripheral vascular resistance can increase by 50% to 60%, while cardiac output can decrease by 30% to 50% Additionally, the loss of the chronotropic action of thyroid hormone directly affects the sinoatrial cells, causing bradycardia. We can also observe anemia due to decreased erythropoietin secretion, which can be another cause of fatigue and decreased endurance [1][21].

In hypothyroidism, there is a reduction in forced vital capacity, forced expiratory flow, and DLCO. Exercise testing parameters such as maximum oxygen consumption %, minute ventilation, tidal volume, and oxygen are also diminished. Additionally, elevated TSH levels were linked to lower percentages of forced expiratory volume in 1 second (FEV1%), FEF25-75%, and DLCO, whereas these parameters had a positive correlation with FT4. This is one of the mechanisms causing decreased endurance [22].

In addition, thyroid hormones play a role in energy availability and consumption in the musculoskeletal system so lack of hormones may cause hypothyroid myopathy which occurs in 30-80% of patients with hypothyroidism. As a result, the patient may develop symptoms like muscle pain, weakness or stiffness [23].

Despite the barriers, physical activity should be promoted among patients with hypothyroidism to improve the cardiovascular and pulmonary function, muscle strength and endurance and to prevent worsening in these fields. Furthermore, physical inactivity is the fourth risk factor for global mortality [20]. In the group with impaired thyroid function, being active is particularly important due to the risk of other diseases associated with a lack of exercise, such as obesity, diabetes, and dyslipidemia [24]. Physical activity is effective in preventing these diseases [25]. As hypothyroid patients often deal with insulin resistance, this is the next reason to be active. Physical activity improves insulin sensitivity by enhancing muscle mitochondrial biogenesis, GLUT4 protein content and glucose uptake, repartitioning intramyocellular lipids and reducing fat mass [26]. Any type of exercise training (aerobic, resistance, and combined) or high-intensity interval training can be performed to improve insulin sensitivity and prevent type 2 diabetes [27].

Flow-mediated endothelium-dependent arterial dilation (FMD), which is impaired in hypothyroidism compared to healthy individuals, appears to improve with regular aerobic exercise. This type of exercise also positively affects lipid profiles by lowering LDL and triglycerides (TG). Furthermore, aerobic exercise has been shown to reduce inflammation, as evidenced by decreased levels of CRP, a marker of inflammation [28]. This anti-inflammatory effect is beneficial especially in Hashimoto's thyroiditis which is an autoimmune disease. Moderate exercise should be performed in this case. On the other hand acute exercise interventions are not effective and can be even pro-inflammatory [29-30].
Another benefit of physical activity in hypothyroidism is improving sleep quality and mitigating symptoms of depression [31].

The role of diet in hypothyroidism

Pharmacotherapy represents the foundation of thyroid disease treatment [32]. However, an expanding body of research and scientific evidence is underscoring the advantageous effects of optimal nutrition on both the trajectory and efficacy of therapy.
The diet of individuals with hypothyroidism should be in accordance with the principles of rational nutrition, providing an adequate intake of essential macronutrients and micronutrients in a properly balanced manner. Carbohydrates, mostly complex, should provide 55-75% of total daily energy needs. Complete proteins 10-15%, fats should not exceed 30%, including a maximum of 10% saturated fats. During the interview process, it is essential to consider the patient's previous dietary habits, educate them on appropriate dietary practices, identify any potential dietary mistakes, and provide guidance on how to rectify these issues [33].
Education in this area and the subsequent introduction of changes in the daily menu of patients have been demonstrated to increase the positive effect of the applied pharmacotherapy, reduce the risk of constipation, and mitigate the severity of inflammation [33].
Subtle changes in the nature of subclinical hypothyroidism have been described in obesity [34-35]. However, it remains uncertain whether obesity per se is the primary driver of these changes or if some form of subclinical hypothyroidism predisposes individuals to obesity. The former hypothesis seems more plausible, given that weight loss has been observed to restore normal thyroid function [36].
For patients with a body mass index (BMI) of 25 or more, a reduction diet is the recommended course of action [37]. It is advised that restrictive diets be avoided, as excessive caloric deprivation has been demonstrated to have profound effects on thyroid function in individuals with an intact hypothalamic–pituitary–adrenal axis (HPA axis) [38]. A study conducted by Vagenakis et al. in 1975 was the first to demonstrate that a lack of caloric intake for four weeks in nine obese subjects resulted in a notable reduction in serum T3 and an increase in reverse triiodothyronine (rT3), which returned to baseline values during a five-day refeeding period [39]. These findings have subsequently been corroborated by contemporary studies [40].
It is recommended that patients with thyroid conditions incorporate foods rich in polyunsaturated fatty acids (PUFAs) into their diets. These fatty acids, particularly omega-3s, have been shown to possess anti-autoimmune properties that may reduce the prevalence of autoimmune thyroiditis globally. Additionally, they may mitigate the risk of developing metabolic and cardiovascular disorders associated with elevated or trending elevated serum TSH levels and thyroid autoimmunity [41].

Important nutrients in hypothyroidism

Iodine, an essential component for the production of thyroid hormones, is not stored in the human body and must be supplied through the diet. It is inadvisable to employ routine iodine supplementation, as excessive intake can precipitate the Wolff-Chaikoff effect, a transient cessation of iodine uptake by the thyroid gland. This phenomenon arises from the introduction of high doses of exogenous iodine into the body, leading to the inhibition of thyroid hormone production and release [42].

Table 1: Recommended Dietary Allowances (RDAs) for Iodine [43]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	110 mcg	110 mcg		
7-12 months	130 mcg	130 mcg		
1-3 years	90 mcg	90 mcg		
4-8 years	90 mcg	90 mcg		
9-13 years	120 mcg	120 mcg		
14-18 years	150 mcg	150 mcg	220 mcg	290 mcg
19+ years	150 mcg	150 mcg	220 mcg	290 mcg

Selenium, a component of the enzyme deiodinase, which induces the conversion of thyroxine to triiodothyronine (T3). Selenium deficiency results in decreased T3 production, oxidative damage to the thyroid, and decreased iodine bioavailability [44].

Table 2: Recommended Dietary Allowances (RDAs) for Selenium [43]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	15 mcg	15 mcg		
7-12 months	20 mcg	20 mcg		
1-3 years	20 mcg	20 mcg		
4-8 years	30 mcg	30 mcg		
9-13 years	40 mcg	40 mcg		
14-18 years	55 mcg	55 mcg	60 mcg	70 mcg
19-50 years	55 mcg	55 mcg	60 mcg	70 mcg
51+ years	55 mcg	55 mcg		

Iron is a component of thyroid iodinating peroxidase, which is responsible for activating the conversion of thyroglobulin to thyroxine and T3. Decreased iron concentrations in the body have been associated with a reduction in T3 and an increase in TSH [45].

Table 3: Recommended Dietary Allowances (RDAs) for Iron [43]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	0,27 mg	0,27 mg		
7-12 months	11 mg	11 mg		
1-3 years	7 mg	7 mg		
4-8 years	10 mg	10 mg		
9-13 years	8 mg	8 mg		
14-18 years	11 mg	15 mg	27 mg	10 mg
19-50 years	8 mg	18 mg	27 mg	9 mg
51+ years	8 mg	8 mg		

It is important to be aware of the potential adverse effects of goitrogenic substances on people with hypothyroidism. It is recommended to avoid these substances or consume them in moderation.

They are found in large quantities in brassica vegetables, legumes (especially soybeans, which contain daidzein and genistein), turnips, rutabagas, peanuts and mustard. These products can be eaten when heated, but soy should be avoided altogether [32-33].

Drug-food interactions

Properly selected doses of levothyroxine are the basic method of treating hypothyroidism.
Studies by Skelin et al. (2017, 2018) proved the influence of many factors on the level of absorption of this drug. The positive effect of taking levothyroxine at selected times of the day (half an hour before breakfast, an hour before the main meal of the day, at bedtime, minimally 2 hours after dinner), and a diet rich in vitamin C on the increased absorption of levothyroxine was found. Conversely, it was proven that the consumption of products such as soy, coffee and grapefruit juice reduced the level of effectively absorbed drug [46-47].
The results of this study are consistent with the conclusions of other research [48-52].

Conclusions

In summary, successful treatment of hypothyroidism requires a multifaceted approach that includes prompt diagnosis, appropriate medications, regular physical activity and a balanced diet. Understanding and addressing the interrelated nature of hypothyroidism and its comorbidities is critical to improving patient outcomes and quality of life. Further research is needed to clarify the direct effects of physical activity on thyroid function and to optimize dietary recommendations for those affected by this condition.

Disclosure

Author's contribution

Conceptualization, Wiktoria Zduńczyk and Anna Dobosz; methodology, Urszula Ciułek and Michalina Dubińska; software, Urszula Ciułek; check, Wiktoria Zduńczyk, Anna Dobosz and Wiktoria Bilska; formal analysis, Michalina Dubińska; investigation, Wiktoria Paduch-Jakubczyk; resources, Wiktoria Paduch-Jakubczyk Anna Dobosz and Wiktoria Bilska; data curation, Michalina Dubińska; writing - rough preparation, Anna Dobosz, Wiktoria Paduch-Jakubczyk and Wiktoria Bilska; writing - review and editing, Wiktoria Zduńczyk, Michalina Dubińska and Urszula Ciułek; visualization, Wiktoria Bilska; supervision, Wiktoria Paduch-Jakubczyk and Urszula Ciułek; project administration, Anna Dobosz and Wiktoria Zduńczyk; receiving funding, no specific funding.

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References
1. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022 May 19;8(1):30. doi: 10.1038/s41572-022-00357-7. Erratum in: Nat Rev Dis Primers. 2022 Jun 10;8(1):39. doi: https://doi.org/10.1038/s41572-022-00357-7 PMID: 35589725.
2. Muraca E, Ciardullo S, Oltolini A, Zerbini F, Bianconi E, Perra S, Villa M, Cannistraci R, Castoldi G, Pizzi P, Manzoni G, Lattuada G, Perseghin G. Resting Energy Expenditure in Obese Women with Primary Hypothyroidism and Appropriate Levothyroxine Replacement Therapy. J Clin Endocrinol Metab. 2020 Apr 1;105(4):dgaa097. doi: https://doi.org/10.1210/clinem/dgaa097 PMID: 32119074.
3. Babić Leko M, Gunjača I, Pleić N, Zemunik T. Environmental Factors Affecting Thyroid-Stimulating Hormone and Thyroid Hormone Levels. Int J Mol Sci. 2021 Jun 17;22(12):6521. doi: https://doi.org/10.3390/ijms22126521 PMID: 34204586; PMCID: PMC8234807.
4. Qiu Y, Liu Q, Luo Y, Chen J, Zheng Q, Xie Y, Cao Y. Causal association between obesity and hypothyroidism: a two-sample bidirectional Mendelian randomization study. Front Endocrinol (Lausanne). 2024 Jan 8;14:1287463. doi: https://doi.org/10.3389/fendo.2023.1287463. PMID: 38260160; PMCID: PMC10801094.
5. Biondi B, Kahaly GJ, Robertson RP. Thyroid Dysfunction and Diabetes Mellitus: Two Closely Associated Disorders. Endocr Rev. 2019 Jun 1;40(3):789-824. doi: https://doi.org/10.1210/er.2018-00163. PMID: 30649221; PMCID: PMC6507635.
6. Song RH, Wang B, Yao QM, Li Q, Jia X, Zhang JA. The Impact of Obesity on Thyroid Autoimmunity and Dysfunction: A Systematic Review and Meta-Analysis. Front Immunol. 2019 Oct 1;10:2349. doi: https://doi.org/10.3389/fimmu.2019.02349. PMID: 31681268; PMCID: PMC6797838.
7. Biondi B. Subclinical Hypothyroidism in Patients with Obesity and Metabolic Syndrome: A Narrative Review. Nutrients. 2023 Dec 27;16(1):87. doi: https://doi.org/10.3390/nu16010087. PMID: 38201918; PMCID: PMC10780356.
8. Triolo TM, Armstrong TK, McFann K, Yu L, Rewers MJ, Klingensmith GJ, Eisenbarth GS, Barker JM. Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. Diabetes Care. 2011 May;34(5):1211-3. doi: https://doi.org/10.2337/dc10-1756. Epub 2011 Mar 23. PMID: 21430083; PMCID: PMC3114477.
9. Nederstigt C, Uitbeijerse BS, Janssen LGM, Corssmit EPM, de Koning EJP, Dekkers OM. Associated auto-immune disease in type 1 diabetes patients: a systematic review and meta-analysis. Eur J Endocrinol. 2019 Feb 1;180(2):135-144. doi: https://doi.org/10.1530/EJE-18-0515. PMID: 30508413.

10. Skov J, Kuja-Halkola R, Magnusson PKE, Gudbjörnsdottir S, Kämpe O, Bensing S. Shared etiology of type 1 diabetes and Hashimoto's thyroiditis: a population-based twin study. Eur J Endocrinol. 2022 May 9;186(6):677-685. doi: https://doi.org/10.1530/EJE-22-0025. PMID: 36321757; PMCID: PMC9175555.
11. Li L, Liu S, Yu J. Autoimmune thyroid disease and type 1 diabetes mellitus: same pathogenesis; new perspective? Ther Adv Endocrinol Metab. 2020 Sep 14;11:2042018820958329. doi: https://doi.org/10.1177/2042018820958329. PMID: 32973994; PMCID: PMC7493255.
12. Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM, Manji N, Allahabadia A, Armitage M, Chatterjee KV, Lazarus JH, Pearce SH, Vaidya B, Gough SC, Franklyn JA. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med. 2010 Feb;123(2):183.e1-9. doi: https://doi.org/10.1016/j.amjmed.2009.06.030. PMID: 20103030.
13. Hemminki K, Li X, Sundquist J, Sundquist K. Familial association between type 1 diabetes and other autoimmune and related diseases. Diabetologia. 2009 Sep;52(9):1820-8. doi: https://doi.org/10.1007/s00125-009-1427-3. Epub 2009 Jun 20. PMID: 19543881.
14.Anaya JM, Castiblanco J, Tobón GJ, García J, Abad V, Cuervo H, Velásquez A, Angel ID, Vega P, Arango A. Familial clustering of autoimmune diseases in patients with type 1 diabetes mellitus. J Autoimmun. 2006 May;26(3):208-14.
doi: https://doi.org/10.1016/j.jaut.2006.01.001. Epub 2006 Feb 24. PMID: 16503115.
15. Jonklaas J. Hypothyroidism, lipids, and lipidomics. Endocrine. 2024 May;84(2):293-300.
doi: https://doi.org/10.1007/s12020-023-03420-9. Epub 2023 Jun 17. PMID: 37329413; PMCID: PMC11076307.
16.Roa Dueñas OH, Koolhaas C, Voortman T, Franco OH, Ikram MA, Peeters RP, Chaker L. Thyroid Function and Physical Activity: A Population-Based Cohort Study. Thyroid. 2021 Jun;31(6):870-875. doi: https://doi.org/10.1089/thy.2020.0517. Epub 2020 Dec 23. PMID: 33198599.
17. Tian L, Lu C, Teng W. Association between physical activity and thyroid function in American adults: a survey from the NHANES database. BMC Public Health. 2024 May 10;24(1):1277. doi: https://doi.org/10.1186/s12889-024-18768-4. PMID: 38730302; PMCID: PMC11084014.
18. Ahn N, Kim HS, Kim K. Exercise training-induced changes in metabolic syndrome parameters, carotid wall thickness, and thyroid function in middle-aged women with subclinical hypothyroidism. Pflugers Arch. 2019 Mar;471(3):479-489. doi: https://doi.org/10.1007/s00424-019-02254-7. Epub 2019 Jan 18. PMID: 30656407.
19. Duñabeitia I, González-Devesa D, Varela-Martínez S, Diz-Gómez JC, Ayán-Pérez C. Effect of physical exercise in people with hypothyroidism: systematic review and meta-analysis. Scand J Clin Lab Invest. 2023 Dec;83(8):523-532. doi: https://doi.org/10.1080/00365513.2023.2286651. Epub 2024 Jan 24. PMID: 37999992.
20. Lankhaar JAC, Kemler E, Hofstetter H, Collard DCM, Zelissen PMJ, Stubbe JH, Backx FJG. Physical activity, sports participation and exercise-related constraints in adult women with primary hypothyroidism treated with thyroid hormone replacement therapy. J Sports Sci. 2021 Nov;39(21):2493-2502. doi: https://doi.org/10.1080/02640414.2021.1940696. Epub 2021 Jun 24. PMID: 34165042.

21. Udovcic M, Pena RH, Patham B, Tabatabai L, Kansara A. Hypothyroidism and the Heart. Methodist Debakey Cardiovasc J. 2017 Apr-Jun;13(2):55-59. doi: https://doi.org/10.14797/mdcj-13-2-55. PMID: 28740582; PMCID: PMC5512679.
22. Sadek SH, Khalifa WA, Azoz AM. Pulmonary consequences of hypothyroidism. Ann Thorac Med. 2017 Jul-Sep;12(3):204-208. doi: https://doi.org/10.4103/atm.ATM_364_16. PMID: 28808493; PMCID: PMC5541969.
23. Fariduddin MM, Haq N, Bansal N. Hypothyroid Myopathy. 2024 Jun 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 30137798.
24. Lankhaar JAC, Kemler E, Stubbe JH, Backx FJG. Physical Activity in Women With Hypothyroidism on Thyroid Hormone Therapy: Associated Factors and Perceived Barriers and Benefits. J Phys Act Health. 2021 Oct 9;18(11):1383-1392. doi: https://doi.org/10.1123/jpah.2021-0230. PMID: 34627125.
25. Dhuli K, Naureen Z, Medori MC, Fioretti F, Caruso P, Perrone MA, Nodari S, Manganotti P, Xhufi S, Bushati M, Bozo D, Connelly ST, Herbst KL, Bertelli M. Physical activity for health. J Prev Med Hyg 2022;63(suppl.3):E150-E159. doi: https://doi.org/10.15167/2421-4248/jpmh2022.63.2S3.2756.
26. Xiang GD, Pu J, Sun H, Zhao L, Yue L, Hou J. Regular aerobic exercise training improves endothelium-dependent arterial dilation in patients with subclinical hypothyroidism. Eur J Endocrinol. 2009 Nov;161(5):755-61. doi: https://doi.org/10.1530/EJE-09-0395. Epub 2009 Sep 8. PMID: 19737872.
27.Mastrototaro, L., & Roden, M. (2021). Insulin resistance and insulin sensitizing agents. Metabolism: clinical and experimental, 125, 154892. doi: https://doi.org/10.1016/j.metabol.2021.154892
28. Oppert JM, Bellicha A, van Baak MA, Battista F, Beaulieu K, Blundell JE, Carraça EV, Encantado J, Ermolao A, Pramono A, Farpour-Lambert N, Woodward E, Dicker D, Busetto L. Exercise training in the management of overweight and obesity in adults: Synthesis of the evidence and recommendations from the European Association for the Study of Obesity Physical Activity Working Group. Obes Rev. 2021 Jul;22 Suppl 4(Suppl 4):e13273. doi: https://doi.org/10.1111/obr.13273. Epub 2021 Jun 2. PMID: 34076949; PMCID: PMC8365734.
29.Luo B, Xiang D, Ji X, Chen X, Li R, Zhang S, Meng Y, Nieman DC, Chen P. The anti-inflammatory effects of exercise on autoimmune diseases: A 20-year systematic review. J Sport Health Sci. 2024 May;13(3):353-367. doi: https://doi.org/10.1016/j.jshs.2024.02.002. Epub 2024 Feb 9. PMID: 38341137; PMCID: PMC11117003.
30.Sharif K, Watad A, Bragazzi NL, Lichtbroun M, Amital H, Shoenfeld Y. Physical activity and autoimmune diseases: Get moving and manage the disease. Autoimmun Rev. 2018 Jan;17(1):53-72. doi: https://doi.org/10.1016/j.autrev.2017.11.010. Epub 2017 Nov 3. PMID: 29108826.
31. Elgayar SL, Elgendy S, Youssef TM. Comparative effects of aerobic, resistance, and combined exercises on depression and sleep quality in women with controlled hypothyroidism. A randomized controlled trial. Advances in Rehabilitation. 2024;38(1):9-19. doi: https://doi.org/10.5114/areh.2024.136292.

32. E. Zakrzewska, M. Zegan., E. Michota-Katulska, D. Szostak-Węgierek. Zalecenia dietetyczna w niedoczynności tarczycy przy współwystępowaniu choroby Hashimoto. BromChemTokskol.2015;48(2):117–127.
33. Jarosz M, Stolińska H, Wolańska D. Żywienie w niedoczynności tarczycy. PZWL, Warszawa 2016: Warszawa.
34. Martins VJB, Filgueiras AR, Almeida VBP, de Moraes RCS, Sawaya AL. Changes in Thyroid and Glycemic Status and Food Intake in Children with Excess Weight Who Were Submitted for a Multi-Component School Intervention for 16 Months. *International Journal of Environmental Research and Public Health*. 2020; 17(11):3825. doi: https://doi.org/10.3390/ijerph17113825.
35. Peeters, R. P. (2017). Subclinical hypothyroidism. *New England Journal of Medicine*, *376*(26), 2556-2565. doi: https://doi.org/10.1056/NEJMcp1611144.
36. Reinehr T. Obesity and thyroid function. Mol Cell Endocrinol. 2010 Mar 25;316(2):165-71. doi: https://doi.org/10.1016/j.mce.2009.06.005. Epub 2009 Jun 18. PMID: 19540303.
37. Redman LM, Ravussin E. Endocrine alterations in response to calorie restriction in humans. Mol Cell Endocrinol. 2009; 299(1): 129–136, doi: https://doi.org/10.1016/j.mce.2008.10.014, indexed in Pubmed: 19007855.
38. Partsalaki I, Markantes GK, Michalaki MA. Low-Glycemic Load Diets and Thyroid Function: A Narrative Review and Future Perspectives. *Nutrients*. 2024; 16(3):347. doi: https://doi.org/10.3390/nu16030347.
39. Vagenakis AG, Burger A, Portnary GI, Rudolph M, O'Brian JR, Azizi F, Arky RA, Nicod P, Ingbar SH, Braverman LE. Diversion of peripheral thyroxine metabolism from activating to inactivating pathways during complete fasting. J Clin Endocrinol Metab. 1975 Jul;41(1):191-4. doi: https://doi.org/10.1210/jcem-41-1-191. PMID: 1150863.
40. Basolo A, Begaye B, Hollstein T, Vinales KL, Walter M, Santini F, Krakoff J, Piaggi P. Effects of Short-Term Fasting and Different Overfeeding Diets on Thyroid Hormones in Healthy Humans. Thyroid. 2019 Sep;29(9):1209-1219. doi: https://doi.org/10.1089/thy.2019.0237. Epub 2019 Aug 9. PMID: 31298652; PMCID: PMC6864752.
41. Benvenga S, Famà F, Perdichizzi LG, Antonelli A, Brenta G, Vermiglio F, Moleti M. Fish and the Thyroid: A Janus Bifrons Relationship Caused by Pollutants and the Omega-3 Polyunsaturated Fatty Acids. Front Endocrinol (Lausanne). 2022 May 27;13:891233. doi: https://doi.org/10.3389/fendo.2022.891233. PMID: 35712237; PMCID: PMC9196333.
42. Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. Lancet Diabetes Endocrinol. 2015; 3(4): 286–295, doi: https://doi.org/10.1016/S2213-8587(14)70225-6, indexed in Pubmed: 25591468.
43. Institute of Medicine (US) Panel on Micronutrients. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington (DC): National Academies Press (US); 2001. Available from: https://www.ncbi.nlm.nih.gov/books/NBK222310/ doi: https://doi.org/10.17226/10026
44. Ventura M, Melo M, Carrilho F. Selenium and Thyroid Disease: From Pathophysiology to Tre- atment. Int J Endocrinol. 2017; 2017: 1297658,
doi: https://doi.org/10.1155/2017/1297658, indexed in Pubmed: 28255299.

45. Luo J, Hendryx M, Dinh P, et al. Association of Iod- ine and Iron with Thyroid Function. Biol Trace Elem Res. 2017; 179(1): 38–44, doi: https://doi.org/10.1007/s12011-017-0954-x, indexed in Pubmed: 28160243.
46. Skelin M, Lucijanić T, Amidžić Klarić D, et al. Factors Affecting Gastrointestinal Absorption of Levothyroxine: A Review. *Clin Ther*. 2017; 39(2): 378–403, doi: https://doi.org/10.1016/j.clinthera.2017.01.005, indexed in Pubmed: 28153426.
47. Skelin M, Lucijanić T, Liberati-Čizmek AM, Klobučar SM, Lucijanić M, Jakupović L, Bakula M, Lončar JV, Marušić S, Matić T, Romić Ž, Dumić J, Rahelić D. Effect of timing of levothyroxine administration on the treatment of hypothyroidism: a three-period crossover randomized study. *Endocrine*. 2018 Nov;62(2):432-439. doi: https://doi.org/10.1007/s12020-018-1686-1 Epub 2018 Jul 24. PMID: 30043093.
48. Perez CL, Araki FS, Graf H, de Carvalho GA. Serum thyrotropin levels following levothyroxine administration at breakfast. Thyroid. 2013 Jul;23(7):779-84. doi: https://doi.org/10.1089/thy.2012.0435 Epub 2013 Jun 21. PMID: 23363386.
49. Otun J, Sahebkar A, Östlundh L, Atkin SL, Sathyapalan T. Systematic Review and Meta-analysis on the Effect of Soy on Thyroid Function. Sci Rep. 2019 Mar 8;9(1):3964. doi: https://doi.org/10.1038/s41598-019-40647-x PMID: 30850697; PMCID: PMC6408586.
50. Lilja JJ, Laitinen K, Neuvonen PJ. Effects of grapefruit juice on the absorption of levothyroxine. Br J Clin Pharmacol. 2005 Sep;60(3):337-41.
doi: doi.org/10.1111/j.1365-2125.2005.02433.x PMID: 16120075; PMCID: PMC1884777.
51. Chon DA, Reisman T, Weinreb JE, Hershman JM, Leung AM. Concurrent Milk Ingestion Decreases Absorption of Levothyroxine. Thyroid. 2018 Apr;28(4):454-457.
doi: https://doi.org/10.1089/thy.2017.0428 Epub 2018 Mar 28. PMID: 29589994; PMCID: PMC5905419.
52. Liu H, Lu M, Hu J, Fu G, Feng Q, Sun S, Chen C. Medications and Food Interfering with the Bioavailability of Levothyroxine: A Systematic Review. Ther Clin Risk Manag. 2023 Jun 23;19:503-523. doi: https://doi.org/10.2147/TCRM.S414460 PMID: 37384019; PMCID: PMC10295503.