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A COMPREHENSIVE REVIEW ON MANAGEMENT OF HASHIMOTO'S DISEASE USING DIETARY APPROACHES

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ABSTRACT

Hashimoto's thyroiditis (HT) is a common autoimmune disorder where the immune system attacks the thyroid gland, resulting in hypothyroidism. First identified by Hakaru Hashimoto in 1912, this condition leads to chronic inflammation and dysfunction of the thyroid, primarily influenced by genetic factors, environmental triggers, and dietary habits. The autoimmune process is characterized by the infiltration of thyroid cells by T-cells and B-cells, which can be worsened by excessive iodine intake, selenium deficiency, and exposure to environmental pollutants. Diagnosing HT typically involves checking for elevated levels of thyroid-stimulating hormone (TSH), decreased free thyroxine (T4), and the presence of anti-thyroid antibodies. Recent research has revealed a link between HT and other autoimmune diseases, particularly rheumatoid arthritis, and highlighted the role of dietary changes, such as gluten-free and nutrient-rich diets, in managing symptoms. The main treatment for HT is levothyroxine, a synthetic version of the thyroid hormone T4, customized for each patient. Current studies are also investigating alternative therapies, including immunotherapies and dietary supplements, to improve thyroid function and regulate autoimmune activity. Given the significant impact of HT on cardiovascular health, collaborative management involving endocrinologists and cardiologists is crucial. This thorough understanding of Hashimoto's disease emphasizes the need for early diagnosis, personalized treatment strategies, and the benefits of dietary adjustments in enhancing patient

outcomes. Future research will delve deeper into the complexities of HT and explore more effective treatment options.

KEYWORDS: Hashimoto's disease, Vitamin D, Selenium, Paleo diet, Levothyroxine.

INTRODUCTION

Humans have two systems for properly coordinating various organs i.e.: the Nervous and Endocrine systems. The endocrine system sends information by releasing hormones in the circulatory system. The immune system is required to identify foreign molecules or organisms entering the body and to fight off them. However, due to certain physical or chemical factors, the immune system loses its ability to identify the body's cells and starts to attack them as if they were foreign objects. This condition is known as an autoimmune disorder.

Goiter is a condition in which the thyroid gland gets enlarged. The etiology behind this was mostly related to the deficiency of iodine in the diet. However, some of them were not related to iodine deficiency. In 1912, Hakaru Hashimoto described this as a lymphomatous thyroid tumor. Years later this condition was recognized as an autoimmune disorder which was named Hashimoto disease.

Thyroiditis is the inflammation of the thyroid gland. Among thyroiditis, Hashimoto thyroiditis is one of the rising autoimmune disorders. It is a chronic condition where the body's antibody attacks the cells of the thyroid gland. As a result of this, the gland is overloaded by the WBCs and becomes scarred. This causes hardening of the gland and it cannot produce enough hormones. The patient is given hormone supplements to maintain the hormone levels in the body.

Hashimoto disease is one of the important underlying causes of hypothyroidism. Along with this, insufficient dietary intake of iodine is one of the most common causes of hypothyroidism. The diagnosis is tough at earlier stages as the patient may show normal as the destruction of the thyroid cells is not continuous. Diagnosis includes the laboratory finding of elevated levels of Thyroid stimulating hormone (TSH), antithyroid peroxidase antibodies (TPO), and decreased levels of free thyroxine (T4).

Etiology

One of the major autoimmune thyroid diseases i.e. Hashimoto's thyroiditis is characterized by the infiltration of thyroid cells by T-cells and B-cells. The exact etiology behind the disease is not known but the factors which encourage the production of the disease are:

Genetic factors: A recent example of a potential private gene contributing to HT involves a previously unidentified splice site variant in the thyroglobulin gene (TG c. 1076-1G > C) associated with exon skipping, producing a variant transcript of TG. This variant was discovered in affected members of an autosomal dominant HT family. It's still uncertain whether this variant produces a thyroglobulin molecule harmful to thyroid cells, triggering autoimmunity, or if it initiates an immune response by other means. The affected members had autoantibodies against both thyroid peroxidase and thyroglobulin. Another report describes a family with autosomal dominant HT linked to a mutation causing haploinsufficiency of the gene encoding A20. A20 haploinsufficiency is known to lead to inflammatory and autoimmune disorders, likely due to its role in regulating T helper 17 (Th17) cells and other immune responses.

Environmental factors

Iodine intake - Excessive iodine consumption can elevate the risk of Hashimoto's disease, particularly in individuals with a genetic predisposition.

Selenium deficiency - Low selenium levels may heighten the risk of Hashimoto's disease by fostering inflammation.

Pollution - Exposure to environmental pollutants, such as tobacco smoke, polychlorinated biphenyls (PCBs), solvents, and heavy metals, can increase the likelihood of developing Hashimoto's disease.

Infections - Chronic infections, especially those caused by viruses and bacteria, can act as triggers for Hashimoto's disease.

Medications - Certain medications, including amiodarone and lithium, can raise the risk of Hashimoto's disease.

Radiation exposure - Being exposed to radiation can increase the risk of developing Hashimoto's disease.

Pesticides, Fungicides, and Herbicides - Contact with these chemicals can elevate the risk of hypothyroidism.

Proximity to petrochemical complexes - Living near petrochemical facilities can raise the risk of Hashimoto's disease.

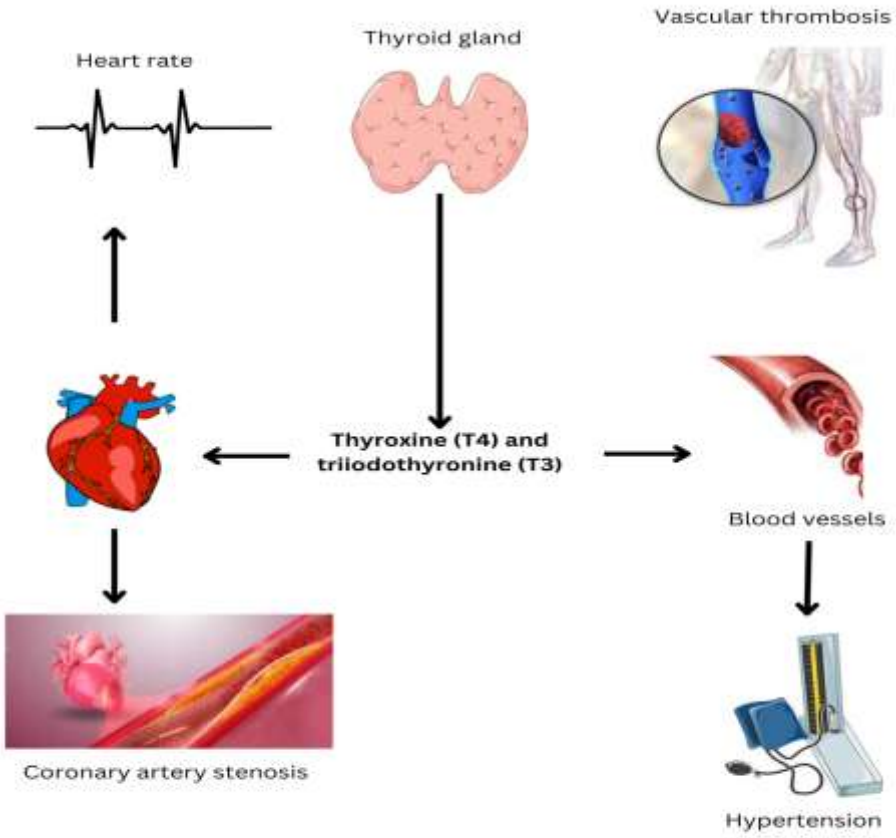
Background study

Rheumatoid arthritis (RA) is an inflammatory disease with an unknown cause, and its link to the thyroid gland, particularly Hashimoto's thyroiditis (HT), is debated. This cross-sectional study, conducted in Najaf from September 2022 to February 2023, involved 140 RA patients (16 males, 124 females, aged 20-60) diagnosed according to ACR/EULAR 2010 criteria. Clinical and laboratory assessments revealed that 32.14% of these patients had HT, including 6.4% with subclinical and 25.7% with overt Hashimoto's thyroiditis. The findings suggest that HT is common among RA patients, highlighting the need for thyroid screening, especially in young women and those with high RA activity.[1]

Krysiak et al.[4] investigated the impact of a gluten-free diet on vitamin D levels in women with Hashimoto's disease, focusing on those with non-celiac gluten sensitivity. The study revealed that while both groups—those on a gluten-free diet and those on a regular diet—experienced improvements in anti-TPO, anti-TG, and vitamin D levels, the regular diet showed superior results. The gluten-free diet appeared to impede vitamin D absorption, potentially limiting its therapeutic effects on thyroid antibodies. Ostrowska et al.[5] observed that a reduction diet based on IgG tests significantly improved body weight, BMI, and body fat in the experimental group compared to the control group, alongside reductions in TSH, anti-TG, and anti-TPO. Pobłocki et al.[6] found that a gluten-free diet in LT4-treated patients reduced TSH but not thyroid hormones or antibodies. Other studies, such as those by Asik et al.[7] demonstrated the potential benefits of lactose-free diets and the effects of Nigella sativa on weight and thyroid markers. Overall, these studies highlight the varying impacts of diet on thyroid function and related parameters in individuals with Hashimoto's disease.[2]

Hashimoto's thyroiditis, a chronic thyroid gland condition, has significant effects on the Cardiovascular system due to its impact on thyroid hormone levels. Thyroid hormones, particularly T3 and T4, play very important roles in regulating heart function, metabolism, and lipid synthesis. In Hashimoto's disease, elevated TSH and reduced T3 and T4 levels, resulting from chronic thyroid inflammation, can damage cardiovascular health. T3 activates the endothelial nitric oxide (NO) signaling pathway, which maintains vascular balance by promoting vasodilation since nitric oxide is a potent vasodilator and reduces vascular constriction. However, in Hashimoto's thyroiditis, this mechanism can be disturbed, leading to increased diastolic blood pressure due to decreased endothelial relaxation.

The condition can accelerate or worsen cardiovascular diseases, presenting symptoms like angina, diastolic hypertension, and various heart rhythm disturbances. Electrocardiographic changes, including QT interval prolongation, can make patients prone to ventricular arrhythmias. Additionally, Hashimoto's thyroiditis may disturb left ventricular function, increase vascular resistance, and cause both systolic and diastolic heart failure, reducing cardiac output by 30-50%. In severe cases, patients may experience coronary artery disease, reduced myocardial contractility, and pericardial effusion, although the latter occurs slowly and is rare enough to allow the heart to adapt. Effective management of cardiovascular complications in Hashimoto's thyroiditis requires interdisciplinary collaboration between endocrinologists and cardiologists.[3]

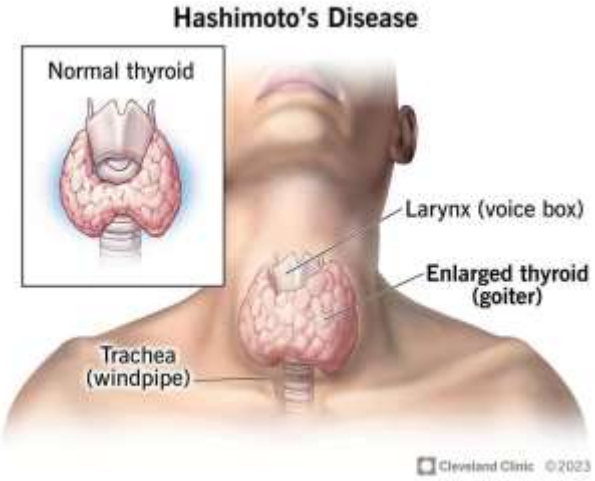


Symptoms and Managaement of hashimoto's disease

Hashimoto disease refers to a disease that occurs due to hypothyroidism, caused by damaging thyroid cells and antibody-mediated immune processes. The illness is named after Dr. Hakaru Hashimoto, who first recognized it in 1912. Other names for Hashimoto's illness are:

- Hashimoto's thyroiditis.
- Chronic autoimmune thyroiditis.
- Lymphocytic thyroiditis.[22]

The thyroid gland is majorly affected by Hashimoto's disease. The autoimmune Hashimoto's disease causes thyroid gland inflammation. The thyroid is a butterfly-shaped gland that is situated immediately below the Adam's apple at the base of the neck, which produces different hormones. Hormones produced by the thyroid gland aid in the regulation of numerous bodily processes.[23]



https://my.clevelandclinic.org/health/diseases/17665-hashimotos-disease

Two thyroid hormones, thyroxine (T4) and triiodothyronine (T3), are produced and secreted by the thyroid gland. The pituitary and thyroid glands cooperate in this process. The gland known as the pituitary, which is situated close to the base of the brain, is responsible for producing, storing, and releasing TSH (Thyroid-stimulating hormone).

In Hashimoto disease, enhanced thyroid-stimulating hormone (TSH) and low free thyroxine (T4) levels are frequently observed together with enhanced antithyroid peroxidase (TPO) antibodies. Since the initial loss of thyroid cells may result in a greater release of thyroid hormone into the bloodstream, patients may initially experience hyperthyroid symptoms. After the antibody reaction has done enough thyroid damage, patients eventually show signs of hypothyroidism. These subtle, fluctuating symptoms have the potential to impact nearly every organ system in the body.

Symptoms

Research by Cellini et al. indicates that about 40 percent of people with autoimmune gastritis also have Hashimoto thyroiditis. The partial or total loss of parietal cells, which impairs the synthesis of hydrochloric acid and intrinsic factors, is a characteristic of chronic autoimmune gastritis (CAG). The patients then experience severe stomach atrophy and pernicious anemia as a result of hypochlorhydria-dependent iron-deficiency anemia.

Primary hypothyroidism is confirmed by a low total T4 or free T4 level in the presence of an increased TSH level. The different blood tests are also used for elevating the Hoshimoto disease - Thyroid stimulating hormone test, Free thyroxine (T4) test, and Antithyroid Antibody test. Eventually, not everyone with hypothyroidism gets Hashimoto's disease but depending on Thyroid levels and blood tests, the disease can be confirmed.

The standard Treatment of hypothyroidism caused by Hashimoto's disease is levothyroxine medication. It is an artificial version of the hormone T4, which is produced by the thyroid gland. Levothyroxine sodium is orally administered daily. It is preferred to take an empty stomach due to the high level of absorption. To prevent less-than-ideal absorption, it shouldn't be administered with calcium or iron supplements, aluminium hydroxide, or proton pump inhibitors. The standard dose of levothyroxine is 1.6 - 1.8 mcg/kg per day, which will vary from patient to patient as per the age criteria.[24]

The most prevalent cause of hypothyroidism globally is an insufficient dietary intake of iodine, which can be prevented by following the proper intake diet explained as follows:

Diagnosis and Evaluation of hashimoto’s disease

Hashimoto’s disease can present with a variety of signs and symptoms, which may overlap with other medical conditions. However, the following methods can be trusted for the diagnosis of the disease. To confirm whether hypothyroidism is responsible for the disease the following tests can be used-

- **TSH Test:** Thyroid-stimulating hormone (TSH) is produced by the pituitary gland. When thyroid hormone levels in the blood are low, the pituitary releases TSH to stimulate the thyroid to produce more hormones. Elevated TSH levels indicate that the thyroid is underactive, pointing to hypothyroidism.

- **T-4 Test:** The primary hormone produced by the thyroid is thyroxine (T-4). A low level of T-4 in the blood further confirms the diagnosis of hypothyroidism and suggests that the issue lies within the thyroid itself.

- **Antibody tests:** Hypothyroidism can result from various underlying conditions. To determine whether Hashimoto's disease is the cause, an antibody test should be conducted. Normally, antibodies in the immune system target harmful foreign substances for destruction. However, in autoimmune disorders like Hashimoto's disease, the immune system by mistake produces antibodies that attack healthy tissues or proteins.[22]

In Hashimoto's disease, the immune system commonly produces antibodies against thyroid peroxidase (TPO), a protein essential for thyroid hormone production. Most individuals with Hashimoto's will have detectable TPO antibodies in their blood.[9]

Evaluation of the disease

Hashimoto's thyroiditis is an autoimmune disorder distinguished by insufficient thyroid hormone production. Biochemical findings typically show elevated thyroid-stimulating hormone (TSH) levels in response to low free T4 levels. A diagnosis of primary hypothyroidism is confirmed when low total or free T4 is accompanied by high TSH levels.

- In integrative and functional medicine, registered medical practitioners may also evaluate free T3 and reverse T3 levels, though this approach is generally not used much.
- The presence of anti-thyroid peroxidase (TPO) and anti-thyroglobulin antibodies is indicative of Hashimoto's thyroiditis, although about 10% of patients may test negative for these antibodies.
- Approximately 30-40% of individuals with Hashimoto's thyroiditis may also present with anemia.
- Other possible findings include reduced glomerular filtration rate (GFR), decreased renal plasma flow, and impaired renal free water clearance, leading to hyponatremia.
- Elevated creatine kinase levels are common, and prolactin levels may also be elevated.
- Patients may experience increased total cholesterol, LDL, and triglyceride levels.
- A thyroid ultrasound can evaluate the size, echotexture, and presence of thyroid nodules, though it is generally not required for diagnosing Hashimoto's thyroiditis in most cases.[10]

Treatment through dietary approach

The primary treatment for Hashimoto's disease is pharmacotherapy, specifically the use of levothyroxine. The dosage is based on the progression of the disease and the patient's body weight. Additionally, a well-balanced diet is crucial. It is important to ensure adequate intake of nutrients that support hormone production by the thyroid gland. Key elements include antioxidants like vitamins A, C, and E, omega-3 fatty acids, and polyphenols, as well as selenium, zinc, iodine, magnesium, and potassium.

Gluten-Free Diet

Gluten is a protein found in wheat, barley, rye, and sometimes oats. It is not fully digested in the human gut, and in genetically predisposed individuals (with HLA-DQ2 or HLA-DQ8), it can trigger an autoimmune response known as celiac disease. This disease affects 1% of the population, causing symptoms like diarrhea, bloating, and nausea. Celiac disease leads to the production of specific antibodies and damages the small intestine, reducing its ability to absorb nutrients like selenium, which is crucial for thyroid hormone metabolism. As a result, celiac disease and Hashimoto's thyroiditis often occur together due to heightened immune sensitivity in both conditions, making a gluten-free diet a recommended approach for Hashimoto's disease.

A gluten-free diet involves avoiding grains such as wheat, rye, barley, and oats, along with medications that may contain these grains as fillers. Given the widespread use of grain products in modern diets, gluten sensitivity, even without celiac disease, is becoming increasingly common, especially in Europeans who consume high levels of gluten. A gluten-free diet is also recommended for patients with dermatitis herpetiformis (Duhring's disease), as their intestinal villi are often partially damaged.

Grain-Free Diet

A grain-free diet is similar to a gluten-free diet, but it also excludes all grains, including Amaranth, Teff, Quinoa, Millet, Oats, Buckwheat. There is limited evidence to suggest that eliminating non-gluten grains benefits overall health. In fact, cutting out these grains may reduce the intake of important nutrients like fibre and selenium, which are essential for individuals with Hashimoto's disease.

Paleo and Autoimmune Paleo Diets

The Paleo diet is designed to copy the eating habits of early humans, focusing on whole, unprocessed foods. It excludes grains, dairy, potatoes, beans, lentils, refined sugar, and refined oils. Instead, the diet encourages the consumption of cage-free and grass-fed meats, vegetables, nuts (except peanuts), seeds, seafood, and healthy fats such as avocado and olive oil.

The Autoimmune Paleo (AIP) diet builds on the Paleo principles but eliminates additional foods that may contribute to inflammation and gut issues. AIP restricts nightshade vegetables (like tomatoes), eggs, nuts, and seeds in an effort to reduce autoimmune flare-ups.

Low glycemic index diet

A low glycemic index (low-GI) diet measures how foods affect blood sugar levels. It is commonly used by individuals with type 2 diabetes and can lower the risk of heart disease while also aiding in weight management.

Nutrient-Dense Diet

For those who prefer focusing on what to include in their diet rather than what to exclude, a nutrient-dense diet may be the best option. This approach focuses on whole foods with a wide variety of colorful fruits and vegetables, healthy fats, lean proteins, and fibre-rich carbohydrates. Recommended foods include:

- Leafy greens (Kale, spinach)
- Fatty fish (Salmon)
- A variety of vegetables (Brussels sprouts, broccoli, carrots, beets, peppers)
- Fruits (Berries, apples, bananas)
- Healthy fats (Avocados, walnuts)
- Lean proteins (Tofu, eggs, beans, fish)
- Fibrous foods (Beans, legumes)

By focusing on these nutrient-rich foods, there is less room for processed or sugary foods. Anti-inflammatory spices like turmeric, ginger, and garlic are also encouraged for their health benefits.[8]

Link between Celiac Disease and Hashimoto's Thyroiditis

Celiac disease is present in 2-7.8% of patients with Hashimoto's disease, a much higher rate than in the general population. The simultaneous occurrence of both diseases may have various causes. Both conditions are autoimmune, with genetic factors playing a significant role in their development.

A key antibody Involved in celiac disease is tissue transglutaminase (TG2), which deaminates gliadin. This enzyme is also found in other tissues, including the thyroid gland, which raises the possibility of cross-reactivity. Additionally, low serum levels of vitamin D3 and selenium, common in celiac patients, can contribute to thyroid dysfunction. The frequent overlap of these two conditions has led researchers to explore the potential benefits of a gluten-free diet as a therapeutic option for patients with chronic lymphocytic thyroiditis. Several studies have been conducted to investigate this connection.[11]

Key nutrients for hypothyroidism

Ensuring a diet rich in essential nutrients is crucial for managing hypothyroidism.

Vitamin D

Vitamin D regulates calcium-phosphate metabolism, crucial for bone health, and also modulates the immune system. Studies show that vitamin D can reduce autoimmune responses by acting on B and T lymphocytes and reducing inflammation. In a 2015 study of 218 individuals with Hashimoto's, 85% were found to have insufficient vitamin D levels. Lower vitamin D levels are commonly seen in Hashimoto's disease (HD) patients, but it's unclear if this is a cause or effect of the disease. Research suggests that vitamin D supplementation may help lower antibodies (anti-TPO Ab and anti-Tg Ab) linked to HD severity, though results vary. Some studies indicate that supplementation reduces these antibodies and TSH levels, but its effects on thyroid hormones like T3 and T4 remain unclear. While evidence supports vitamin D supplementation as a low-cost, safe adjunctive therapy, especially for patients with low disease activity, larger studies are needed to determine the optimal dose and duration for HD patients.

Anyone diagnosed with Hashimoto's should ensure they have their vitamin D levels tested. Vitamin D can be naturally produced by the body through sun exposure or obtained from food and supplements. Due to modern lifestyles, where many adults spend most of their time indoors, vitamin D deficiency is increasingly common.

According to the National Institutes of Health (NIH), "approximately 5–30 minutes of sun exposure between 10 AM and 3 PM at least twice a week to the face, arms, legs, or back without sunscreen usually leads to sufficient vitamin D production."

For those unable to get consistent sun exposure, taking vitamin D supplements is recommended, as very few foods naturally provide sufficient amounts of this nutrient.

Selenium

Selenium is an essential trace mineral that plays a vital role in brain function, immune health, and fertility with antioxidant properties and a role in enzyme regulation. It aids in hormone conversion and protects thyroid cells from damage. Selenium deficiency can lead to thyroid damage and autoimmune thyroiditis by weakening immune function and increasing inflammation. Low selenium levels are frequently seen in individuals with Hashimoto's disease. The thyroid gland stores the highest amount of selenium in the body, and research has shown that selenium supplementation may benefit people with thyroid dysfunction, including Hashimoto's. Top food sources of selenium include: Brazil nuts, Halibut, Tuna, Oysters, Sardines, Lobster, Liver, Grass-fed beef, Sunflower seeds, Eggs.[8]

Protein's role in thyroid health

Thyroid hormone levels are regulated by feedback mechanisms in the hypothalamus-pituitary-thyroid (HPT) axis, with thyrotropin-releasing hormone (TRH) playing a central role. TRH secretion is influenced by metabolic signals like leptin, insulin, and ghrelin, making diet important for HPT function. Protein intake, in particular, affects thyroid hormone balance. Low-protein diets, often seen in autoimmune thyroid diseases like Hashimoto's, can disrupt the HPT axis, damage the thyroid, and reduce iodine absorption. Proper protein intake (15-25% of daily calories) helps maintain thyroid health and function, especially in Hashimoto's patients.[15]

How do Diet and Nutrition affect hashimoto's disease?

The thyroid requires iodine, a mineral found in certain foods, to produce thyroid hormones. However, if you have Hashimoto's disease or other autoimmune thyroid disorders, you may be more sensitive to the negative effects of iodine. Consuming large amounts of iodine-rich foods—such as kelp, dulse, other types of seaweed, or iodine-containing medications—can trigger or worsen hypothyroidism. Iodine supplements can have a similar impact.

It is important to discuss the following with your healthcare team:

- Which foods and drinks you should limit or avoid
- Whether you should take iodine supplements
- Any cough syrups you use that might contain iodine

If someone is pregnant, it's essential to get enough iodine, as her baby receives iodine from her diet. However, excessive iodine can also cause issues, such as a goitre in the baby. The doctor should determine the appropriate amount of iodine during pregnancy.[13]

Who is at risk for hashimoto's disease?

Several factors can increase the likelihood of developing Hashimoto's thyroiditis:

Gender: Women are more prone to the condition. It sometimes starts during pregnancy and may improve during pregnancy, but often returns after childbirth.

Age: The condition typically occurs between the ages of 30 and 60, although it can also affect younger individuals.

Family history: A family history of Hashimoto's thyroiditis increases the risk, although no specific gene has been identified as the cause.

Other autoimmune diseases: Conditions such as rheumatoid arthritis, Addison's disease, and type 1 diabetes raise the risk of developing Hashimoto's thyroiditis. Additionally, having Hashimoto's increases the risk of other autoimmune diseases.

Pharmacological treatment

Standard treatments for Hashimoto's thyroiditis may not work for all patients, leading to the exploration of alternative therapies:

- **Levothyroxine:** The primary hormone replacement therapy for hypothyroidism in Hashimoto's, it's tailored to each patient and adjusted based on thyroid hormone levels.
- **Corticosteroids:** Drugs like Prednisone may reduce inflammation short-term, but long-term use has significant risks.
- **Immunotherapies:** Drugs like Rituximab, Etanercept, and Tocilizumab target immune system components to reduce autoimmune responses. Early results show promise, but larger studies are needed.
- **Thyroid hormone analogs:** Tiratricol, a thyroid hormone analog, may help compensate for hormone deficiency and modulate autoimmune response, though more research is required.
- **Selenium supplements:** Selenium may improve thyroid hormone metabolism, but its effects require further study.

- **Vitamin D:** In vitamin D-deficient patients, supplementation may improve thyroid function, though further research is necessary.
- **Mesenchymal stem cell therapy:** Early research suggests stem cells could help modulate the immune system and repair thyroid tissue, but human trials are still in early stages.
- **Metformin:** This hypoglycemic medication may reduce thyroid antibodies and TSH levels by modulating immune responses.
- **DTE or LT4/T3 combination therapy:** Some patients benefit from combination therapies when levothyroxine alone is insufficient.
- **Surgical intervention:** Thyroidectomy may be considered for severe cases, but hormone replacement therapy is still required afterward.[14]

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