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Hashimoto's Thyroiditis: Pathophysiology, Clinical Manifestations, Diagnosis, and Nursing Management-An Updated Review.

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Abstract

Background: Hashimoto's thyroiditis is a chronic autoimmune disorder characterized by immune-mediated destruction of thyroid follicular cells, leading to progressive thyroid dysfunction and, frequently, hypothyroidism. It is one of the most common causes of acquired hypothyroidism and requires long-term clinical monitoring and management.

Aim: This review aims to describe the etiology, epidemiology, pathophysiology, histopathological features, clinical manifestations, diagnostic evaluation, treatment, and nursing management of Hashimoto's thyroiditis.

Methods: Relevant medical literature and clinical references were reviewed to summarize current knowledge regarding disease mechanisms, risk factors, diagnostic approaches, therapeutic strategies, prognosis, and potential complications. Emphasis was placed on the clinical and nursing implications of disease assessment, treatment, patient education, and follow-up.

Results: Hashimoto's thyroiditis results from interactions between genetic susceptibility and environmental factors that trigger autoimmune responses against thyroid antigens, particularly thyroid peroxidase and thyroglobulin. Clinical manifestations range from an asymptomatic euthyroid state to overt hypothyroidism, with occasional transient thyrotoxicosis. Diagnosis relies on thyroid function testing, thyroid autoantibody measurements, and ultrasonography when indicated. Levothyroxine remains the standard treatment for established hypothyroidism, while correction of nutritional deficiencies and appropriate dietary practices may support general health. Potential complications include reproductive disturbances, thyroid nodules, and, rarely, primary thyroid lymphoma.

Conclusion: Early diagnosis, individualized treatment, regular thyroid function monitoring, and effective patient education are essential for controlling symptoms, preventing complications, and maintaining quality of life.

Keywords: Hashimoto's thyroiditis; autoimmune thyroiditis; hypothyroidism; thyroid autoantibodies; levothyroxine; diagnosis; nursing management.

Introduction

Hashimoto's thyroiditis (HT), also known as chronic autoimmune thyroiditis or chronic lymphocytic thyroiditis, is a common organ-specific autoimmune disorder characterized by progressive destruction of thyroid follicular cells through cell-mediated and antibody-mediated immune mechanisms. It represents one of the leading causes of hypothyroidism, particularly in developed countries, where iodine deficiency is less prevalent. The disease develops when the immune system mistakenly recognizes thyroid tissue as a foreign target, resulting in the production of antithyroid antibodies and activation of autoreactive T lymphocytes. These immune responses cause chronic inflammation, damage to thyroid follicular cells, and gradual replacement of normal thyroid tissue with fibrotic tissue. As the disease progresses, the thyroid gland becomes less capable of producing sufficient thyroid hormones, eventually resulting in hypothyroidism in many affected individuals.[1,2] Hashimoto's thyroiditis was first described in 1912 by the Japanese physician Haruto Hashimoto, who identified characteristic pathological changes in thyroid tissue obtained from patients with enlarged thyroid glands. He referred to the condition as "struma lymphomatosa" because of the extensive lymphocytic infiltration observed within the thyroid gland. This finding established the foundation for recognizing Hashimoto's thyroiditis as a distinct autoimmune

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thyroid disorder. It is currently classified among autoimmune thyroid diseases, together with Graves' disease, although the two conditions differ in their underlying immune mechanisms and clinical manifestations.[2,3]

Hashimoto's thyroiditis predominantly affects women, with reported female-to-male ratios ranging from 7:1 to 10:1. Although the disease can develop at any age, its occurrence increases with advancing age, and many cases are diagnosed between 45 and 55 years. Genetic susceptibility, environmental exposures, hormonal influences, and individual immune responses contribute to disease development. The condition is also associated with iodine intake, with higher incidence reported in populations where iodine deficiency is less common.[2,4,5] Clinically, Hashimoto's thyroiditis may present with an enlarged thyroid gland (goiter), fatigue, weight gain, cold intolerance, constipation, dry skin, and other manifestations of reduced thyroid hormone production. However, some patients remain asymptomatic during the early stages, and the disease may be detected incidentally through thyroid function tests or the presence of thyroid autoantibodies. Furthermore, Hashimoto's thyroiditis may occur independently or in association with autoimmune polyglandular syndromes, reflecting the broader relationship between autoimmune disorders. Changes between Graves' disease and Hashimoto's thyroiditis have also been reported, suggesting shared autoimmune mechanisms despite their different clinical presentations.[6–10] From a nursing perspective, understanding Hashimoto's thyroiditis is important for early recognition of symptoms, monitoring thyroid function, supporting medication adherence, providing patient education, and preventing complications associated with untreated hypothyroidism.

Etiology

The exact etiology of Hashimoto's thyroiditis (HT) remains incompletely understood. However, current evidence indicates that the disease develops through a complex interaction between genetic susceptibility, environmental exposures, nutritional factors, and abnormalities in immune regulation. These factors contribute to the loss of immune tolerance to thyroid-specific antigens, resulting in the activation of autoreactive T lymphocytes and the production of thyroid-directed autoantibodies. The resulting autoimmune response causes chronic inflammation and progressive destruction of thyroid follicular cells. Although genetic predisposition plays an important role, environmental and nutritional factors may influence disease initiation, progression, and clinical severity.

Genetic Factors

Genetic susceptibility is an important determinant of Hashimoto's thyroiditis. The disease frequently occurs in multiple members of the same family, suggesting an inherited predisposition to autoimmune thyroid disorders. Familial clustering may involve both Hashimoto's thyroiditis and Graves' disease, indicating that these conditions share certain genetic and immunological mechanisms. A Danish twin study reported approximately 50% concordance for Hashimoto's thyroiditis and 80% concordance for thyroid antibody positivity among monozygotic twins, supporting the contribution of hereditary factors to disease development.[11,12] Several genetic variations have been associated with increased susceptibility to Hashimoto's thyroiditis. These include genes within the human leukocyte antigen (HLA) complex, which regulates antigen presentation and immune recognition. Other important susceptibility genes include CD40, FOXP3, CD25, CTLA-4, and PTPN22, which participate in T-cell activation, immune regulation, and the maintenance of self-tolerance. Furthermore, thyroid-specific genes encoding the thyroid-stimulating hormone (TSH) receptor and thyroglobulin may contribute to autoimmune recognition of thyroid tissue. The disease also occurs more frequently in individuals with certain chromosomal disorders, particularly Turner syndrome and Down syndrome, suggesting that chromosomal abnormalities may influence immune regulation and autoimmune susceptibility.[11–14]

Environmental Factors

Although genetic factors contribute substantially to disease susceptibility, environmental exposures are also important. The incomplete concordance of Hashimoto's thyroiditis among genetically identical twins demonstrates that inherited susceptibility alone cannot explain disease development. Environmental conditions, nutritional status, infections, and other external exposures may interact with genetic factors and trigger autoimmune responses in susceptible individuals.[15]

Hygiene Hypothesis

The hygiene hypothesis suggests that reduced exposure to microorganisms during childhood may influence the development of immune regulation. Individuals living in environments with high sanitation standards and limited exposure to microbial agents may have a greater tendency to develop certain allergic and autoimmune conditions. Reduced microbial stimulation may affect the development of immune tolerance and the balance between different immune cell populations, potentially increasing susceptibility to autoimmune thyroid diseases, including Hashimoto's thyroiditis.[16]

Iodine Status

Iodine is an essential element required for thyroid hormone synthesis. However, both insufficient and excessive iodine intake may adversely affect thyroid health and autoimmune regulation. Mild iodine deficiency has been associated with a lower

prevalence of Hashimoto's thyroiditis in some populations. In contrast, excessive and prolonged iodine exposure has been linked to an increased prevalence of thyroid autoimmunity. One proposed mechanism involves increased iodination of thyroglobulin, which may enhance its immunogenicity and promote recognition by the immune system. Severe iodine deficiency may also contribute to thyroid autoimmunity through mechanisms involving thyroid stimulation, cellular stress, and changes in thyroid antigen expression.[17–20]

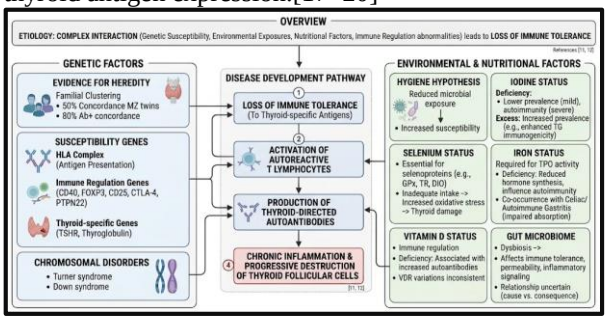


Figure-1: Etiology of Hashimoto's Thyroiditis.

Selenium Status

Selenium is an essential micronutrient involved in thyroid hormone metabolism and protection against oxidative stress. It is incorporated into several important selenoproteins, including iodothyronine deiodinases, glutathione peroxidases, and thioredoxin reductases. These enzymes participate in thyroid hormone activation and inactivation, cellular metabolic regulation, maintenance of redox balance, and protection of thyroid follicular cells against damage caused by reactive oxygen species.[21–24] Inadequate selenium intake may increase oxidative stress and interfere with normal thyroid function, potentially contributing to autoimmune thyroid inflammation. A systematic review and meta-analysis published in 2024 reported reductions in thyroid antibody concentrations following selenium supplementation. Reductions in TSH levels were also observed, with moderate certainty of evidence. These findings suggest that selenium may influence certain biochemical markers of Hashimoto's thyroiditis, although its clinical benefits and appropriate use require further investigation.[25]

Iron Status

Iron is necessary for normal thyroid function because thyroid peroxidase (TPO), an essential enzyme involved in thyroid hormone synthesis, contains a heme group. Iron deficiency may reduce TPO activity, interfere with thyroid hormone production, and potentially influence thyroid autoimmunity. Patients with Hashimoto's thyroiditis may also have an increased risk of iron deficiency because of associated autoimmune conditions, particularly celiac disease and autoimmune gastritis, which can impair intestinal iron absorption.[17,26–28] Women of reproductive age represent another population at increased risk of iron deficiency because of menstrual blood loss. Therefore, evaluating iron status may be relevant when assessing patients with Hashimoto's thyroiditis, particularly those presenting with fatigue, weakness, or other symptoms that may overlap with hypothyroidism.[29]

Vitamin D Status

Vitamin D plays an important role in immune regulation and the maintenance of immune tolerance. It influences the activity of several immune cells, including T lymphocytes, B lymphocytes, and antigen-presenting cells. Vitamin D deficiency has been associated with increased thyroid autoantibody concentrations, suggesting a possible relationship between inadequate vitamin D status and the development or progression of Hashimoto's thyroiditis. Genetic variations in the vitamin D receptor have also been investigated as potential susceptibility factors. However, findings concerning the association between vitamin D receptor polymorphisms and autoimmune thyroid disease remain inconsistent.[30–33]

Role of the Gut Microbiome

The gut microbiome contributes to immune system development, intestinal barrier integrity, inflammatory regulation, and metabolic processes. It may also influence thyroid hormone metabolism through interactions involving microbial enzymes and nutrient availability. Alterations in the composition or function of intestinal microorganisms, commonly described as gut dysbiosis, have been proposed as potential contributors to autoimmune thyroid diseases. Changes in microbial populations may influence immune tolerance, intestinal permeability, and inflammatory signaling, potentially promoting autoimmune responses against thyroid tissue.[34–37] Nevertheless, the relationship between gut microbiome alterations and Hashimoto's thyroiditis remains uncertain. It is not yet established whether intestinal dysbiosis precedes autoimmune thyroid disease or develops as a consequence of the disease or its associated metabolic changes. A cross-sectional study involving euthyroid individuals found no substantial differences in gut microbiome alpha-diversity or beta-diversity between participants with and without thyroid peroxidase antibodies. These findings indicate that further longitudinal and mechanistic investigations are necessary to clarify the contribution of intestinal microorganisms to thyroid autoimmunity.[38]

Epidemiology

Hashimoto's thyroiditis is the most common cause of hypothyroidism in the United States and in regions where dietary iodine intake is adequate. Its prevalence varies across geographical regions and populations, reflecting differences in genetic susceptibility, environmental exposures, iodine consumption, and diagnostic practices.[39] A systematic review and meta-analysis involving studies from several countries estimated the global prevalence

of Hashimoto's thyroiditis at approximately 7.5%, with a higher prevalence of 11.4% reported in low- and middle-income regions. The disease demonstrates a marked gender difference, affecting women approximately four times more frequently than men.[40] This predominance may be associated with differences in hormonal influences, genetic susceptibility, and immune system regulation between sexes. Thyroid autoantibodies are also relatively common in the general population, with approximately 10% of individuals in the United States showing positive thyroid antibody tests. Studies have reported thyroid antibody prevalence ranging from 5% to 20%, depending on the population examined and the diagnostic methods used.[41–45] Pregnancy represents another important population for epidemiological assessment because thyroid autoimmunity may influence maternal thyroid function and pregnancy outcomes. Thyroid peroxidase antibodies are detected in approximately 5%–14% of pregnant women, while thyroglobulin antibodies occur in approximately 3%–18%. These findings highlight the importance of recognizing thyroid autoimmunity during pregnancy and monitoring thyroid function when clinically indicated.[46]

Pathophysiology

Hashimoto's thyroiditis is an organ-specific autoimmune disorder characterized by chronic lymphocytic infiltration, inflammation, and progressive destruction of thyroid follicular cells. Histopathological examination typically reveals extensive lymphocyte infiltration, formation of lymphoid follicles, follicular atrophy, and varying degrees of thyroid tissue fibrosis. The disease develops through interactions between cellular and humoral immune mechanisms involving T lymphocytes and B lymphocytes. These immune responses progressively damage thyroid tissue, impair thyroid hormone synthesis, and may eventually result in hypothyroidism.[47] B lymphocytes contribute to the pathogenesis of Hashimoto's thyroiditis through the production of autoantibodies directed against thyroid-specific antigens. Thyroid peroxidase antibodies (TPOAb) are the most frequently detected autoantibodies, occurring in more than 90% of affected individuals. These antibodies target thyroid peroxidase, an enzyme essential for thyroid hormone synthesis. Thyroglobulin antibodies (TgAb) are also commonly detected, occurring in approximately 50%–80% of patients, and target thyroglobulin, a protein involved in thyroid hormone production.[48–50] Another group consists of thyroid-stimulating hormone receptor antibodies (TSHRAb), which may have stimulating, blocking, or neutralizing effects. Blocking antibodies predominate in Hashimoto's thyroiditis and interfere with TSH-mediated thyroid stimulation. In rare cases, stimulating antibodies may develop, potentially contributing to thyroid eye disease or a clinical transition toward Graves' disease.[51–55]

T lymphocytes play a central role in thyroid inflammation and follicular cell destruction. CD8+ cytotoxic T cells infiltrate thyroid tissue and directly damage follicular cells through cytotoxic mechanisms, contributing to cellular apoptosis and progressive loss of functional thyroid tissue.[56] CD4+ helper T cells also participate in disease progression by activating macrophages, stimulating B lymphocytes, and promoting inflammatory responses. Several CD4+ T-cell subsets, including Th1, Th2, Th17, and regulatory T cells (Tregs), influence the development and regulation of thyroid autoimmunity.[47,57] An imbalance between these T-cell populations contributes to the breakdown of immune tolerance. Th1 cells are increased in Hashimoto's thyroiditis and promote inflammation through the release of proinflammatory cytokines. Conversely, regulatory T cells normally suppress excessive immune responses and maintain tolerance to self-antigens. Reduced Treg activity or numbers may impair this protective mechanism, allowing autoreactive lymphocytes to persist and attack thyroid tissue.[58] The combined effects of autoantibody production, cytotoxic T-cell activity, and chronic inflammatory responses result in progressive destruction of thyroid follicular cells. As functional thyroid tissue declines, the gland becomes increasingly unable to produce adequate amounts of thyroxine (T4) and triiodothyronine (T3), leading to elevated TSH concentrations and the development of clinical hypothyroidism.

Histopathology

The characteristic histopathological feature of Hashimoto's thyroiditis is extensive lymphocytic infiltration of the thyroid gland, accompanied by progressive destruction of thyroid follicular cells. This inflammatory infiltration consists mainly of lymphocytes and plasma cells, with the occasional presence of macrophages and multinucleated giant cells. These immune cells accumulate within thyroid tissue and contribute to chronic inflammation, follicular damage, and gradual loss of normal thyroid architecture.[59,60] Another characteristic finding is the formation of lymphoid follicles, sometimes containing germinal centers, which reflect ongoing local immune activity. Thyroid follicular cells may undergo metaplastic changes, resulting in the development of Hürthle cells, also known as Askanazy cells. These cells are characterized by abundant granular eosinophilic cytoplasm resulting from increased mitochondrial content. Their presence is considered an important microscopic feature of chronic autoimmune thyroiditis.[61,62] Progressive inflammatory damage is frequently associated with varying degrees of interstitial fibrosis, which may replace normal thyroid parenchyma and contribute to reduced glandular function. Histopathological

variations of Hashimoto's thyroiditis include atrophic and fibrotic forms, which are characterized by marked follicular loss and extensive connective tissue replacement.[63] Other related forms include Riedel thyroiditis, characterized by extensive fibrosis involving the thyroid gland and potentially surrounding structures, and immunoglobulin G4 (IgG4)-related thyroiditis, which represents a distinct fibroinflammatory pattern associated with increased IgG4-positive plasma cells.[64–68] These histopathological changes reflect the chronic autoimmune process responsible for progressive thyroid tissue destruction and the development of hypothyroidism.

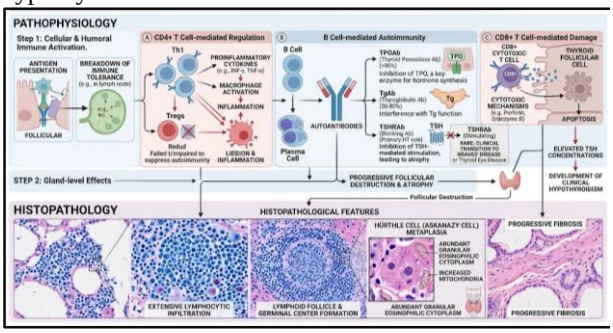


Figure-2: Pathophysiology and Histopathology of Hashimoto's Thyroiditis.

History and Physical Examination

The clinical presentation of Hashimoto's thyroiditis varies considerably depending on the stage of the disease, the degree of thyroid tissue destruction, and the resulting changes in thyroid hormone production. Patients may remain asymptomatic for several years, develop transient hyperthyroidism, or present with subclinical or overt hypothyroidism. Clinical assessment should include a detailed medical history, evaluation of thyroid-related symptoms, and physical examination to identify possible complications. A small proportion of patients initially develop transient hyperthyroidism, known as Hashitoxicosis. This condition results from inflammatory destruction of thyroid follicular cells, causing the release of previously stored thyroid hormones into the bloodstream. Patients may experience palpitations, nervousness, sweating, heat intolerance, and weight loss. Unlike Graves' disease, this hyperthyroid phase is usually temporary and may eventually progress to permanent hypothyroidism.[69–71] Rarely, patients with established Hashimoto's thyroiditis may develop Graves' disease after years of hypothyroidism because of changes in thyroid-stimulating receptor antibody activity.[72–74] Most patients remain euthyroid during the early stages, with normal thyroid function despite the presence of thyroid autoantibodies. However, approximately 20%–30% eventually develop hypothyroidism as thyroid tissue destruction progresses.[75] Subclinical hypothyroidism is characterized by elevated serum thyroid-stimulating hormone (TSH), usually below 10 mIU/L, with normal circulating thyroxine (T4) and triiodothyronine (T3) concentrations.[76] In contrast, overt hypothyroidism is associated with elevated TSH, commonly above 10 mIU/L, and reduced T4 concentrations. Typical manifestations include fatigue, unexplained weight gain, cold intolerance, constipation, menstrual irregularities, hair loss, brittle nails, depression, impaired concentration, and memory difficulties. Physical findings may include periorbital puffiness, ankle edema, hoarseness, muscle weakness, joint pain, and peripheral neuropathy.[77–79]

Thyroid inflammation may occasionally present as painful or painless thyroiditis, sometimes accompanied by transient thyrotoxicosis. Most cases are painless and resolve within several months, although recurrent or prolonged painful presentations have been reported.[80–83] In women, thyroid autoimmunity may also be identified during investigations for infertility, recurrent miscarriage, or difficulties with assisted reproductive procedures.[84–86] Postpartum thyroiditis is another recognized presentation, particularly among women with underlying Hashimoto's thyroiditis. It commonly develops around six months after delivery but may occur anytime during the first postpartum year. The condition is associated with increased autoimmune activity following pregnancy and is usually transient, although some women develop permanent hypothyroidism.[87,88] Chronic thyroid inflammation may also result in thyroid nodules, which occur in approximately 20%–30% of affected individuals. Thyroid enlargement, with or without nodules, may cause dysphagia, dyspnea, dysphonia, chronic cough, or neck pressure.[87] Additionally, thyroid eye disease occurs in up to 6% of patients, particularly in association with stimulating TSH receptor antibodies.[54,89,90]

Evaluation

Laboratory and Imaging Studies

The evaluation of Hashimoto's thyroiditis involves laboratory investigations to assess thyroid function, detect autoimmune activity, and identify associated metabolic or nutritional abnormalities. Thyroid function tests, particularly serum thyroid-stimulating hormone (TSH) and thyroxine (T4), are essential for determining the functional status of the thyroid gland. Elevated TSH with normal T4 indicates subclinical hypothyroidism, whereas elevated TSH accompanied by reduced T4 suggests overt hypothyroidism. Thyroid autoantibody testing supports the diagnosis of autoimmune thyroiditis. Thyroid peroxidase antibodies (TPOAb) are detected in more than 90% of patients, while thyroglobulin antibodies (TgAb) are present in approximately 50% to 80% of cases. Higher antibody levels are associated with autoimmune thyroid activity and an increased likelihood of developing overt hypothyroidism. Patients with positive thyroid antibodies are also more likely to have a family history of thyroid disease and increased thyroid gland size. In patients presenting

with thyroid eye disease, TSH receptor antibodies should be measured to assess possible coexisting Graves' disease.[91,92] Additional laboratory investigations may identify associated conditions and complications. Iron studies, including serum iron and ferritin, are appropriate when patients present with symptoms of iron deficiency or gastrointestinal complaints. This is particularly relevant because Hashimoto's thyroiditis is associated with an increased prevalence of celiac disease and autoimmune atrophic gastritis. Vitamin D levels may also be assessed because deficiency occurs more frequently in individuals with thyroid disorders.[93] A fasting lipid profile can identify dyslipidemia, particularly elevated low-density lipoprotein cholesterol, which may develop as a consequence of reduced thyroid hormone activity. Creatine kinase measurement may be considered in patients with unexplained muscle pain or weakness, as hypothyroidism can occasionally cause elevated levels. Thyroid ultrasonography is indicated when physical examination reveals gland enlargement, palpable nodules, or suspected structural abnormalities. It is also appropriate when patients report compressive symptoms, such as difficulty swallowing or breathing. Ultrasound can demonstrate characteristic features of autoimmune thyroiditis, including diffuse hypoechogenicity and heterogeneous thyroid tissue. These findings help assess gland structure and identify nodules requiring further investigation.

Treatment and Management

Current clinical guidelines focus on controlling thyroid dysfunction, relieving symptoms, preventing complications, and maintaining an appropriate quality of life. Hashimoto's thyroiditis has no established curative treatment. Management depends on thyroid function, clinical manifestations, age, pregnancy status, associated conditions, and individual patient needs.

Thyroid Hormone Replacement

Levothyroxine sodium is the standard treatment for hypothyroidism caused by Hashimoto's thyroiditis. It replaces the thyroxine that the damaged thyroid gland can no longer produce in sufficient quantities. Levothyroxine has a half-life of approximately seven days, allowing once-daily administration. The usual full replacement dose in adults is approximately 1.4–1.8 µg/kg/day, although the required dose varies according to body weight, age, residual thyroid function, disease severity, and other clinical factors. For optimal absorption, levothyroxine should be taken orally in the morning on an empty stomach, preferably 30–60 minutes before breakfast. Patients should avoid taking it simultaneously with calcium or iron supplements, aluminum-containing antacids, and certain other medications that interfere with absorption. Proton pump inhibitors may also affect levothyroxine absorption in some patients. Consistent administration and appropriate separation from interacting products help maintain stable thyroid hormone levels. Treatment initiation and dose selection should be individualized. Adults younger than 60 years without cardiovascular disease may receive a full replacement dose when overt hypothyroidism is present. Older adults and patients with coronary artery disease or other cardiovascular conditions generally require lower initial doses to reduce the risk of cardiac complications. A starting dose of approximately 25 µg/day may be appropriate in patients aged 60 years or older, followed by gradual adjustment according to clinical response and laboratory findings. TSH should generally be reassessed six to eight weeks after starting treatment or changing the dose. Once thyroid function stabilizes, periodic monitoring is required. Pregnancy increases thyroid hormone requirements, and women already receiving levothyroxine may need an early dose increase, commonly around 30%, followed by regular monitoring throughout pregnancy. Patients with intestinal disorders, short-bowel syndrome, or other causes of malabsorption may require higher doses or further assessment of absorption. Maintaining appropriate thyroid hormone levels is essential to support maternal health and fetal development.[94]

Treatment in Euthyroid Women

The use of levothyroxine in euthyroid women with thyroid autoantibodies remains a subject of clinical discussion, particularly among women planning pregnancy, experiencing recurrent pregnancy loss, or undergoing assisted reproductive procedures. Some experts have proposed treatment when TSH exceeds 2.5 mIU/L, especially in women with a history of pregnancy loss or infertility.[76] However, recommendations differ because evidence has not consistently demonstrated improved fertility or pregnancy outcomes. The American Society for Reproductive Medicine recommends against routine levothyroxine treatment in women with TSH levels below 4 mIU/L because available evidence does not establish reductions in miscarriage risk or improvements in fertility, obstetric outcomes, or childhood development.[95] Therefore, treatment decisions should consider TSH concentration, thyroid antibody status, reproductive history, pregnancy plans, and individual clinical circumstances. Regular thyroid function monitoring remains important in women with autoimmune thyroiditis who are planning pregnancy or become pregnant.

Selenium Supplementation

Selenium contributes to thyroid hormone metabolism and antioxidant defense through its role in selenoproteins. Its potential use in Hashimoto's thyroiditis has been investigated because oxidative stress and autoimmune activity contribute to thyroid tissue damage. Systematic reviews and meta-analyses

have reported modest improvements in thyroid function parameters and reductions in thyroid antibody concentrations, particularly among individuals who are not receiving thyroid hormone replacement.[25,96] Some studies suggest that selenium supplementation at doses of 50–100 µg/day may be beneficial, especially in populations with inadequate selenium intake.[97] A study involving 412 patients with hypothyroidism associated with Hashimoto's thyroiditis reported improvements in quality-of-life measures following supplementation with 200 µg/day.[98] Nevertheless, evidence remains insufficient to recommend routine selenium supplementation for all patients. Excessive selenium intake can cause toxicity; therefore, supplementation should be considered according to dietary intake, nutritional status, and clinical assessment. Selenium should not replace levothyroxine in patients with established hypothyroidism.

Management of Iron Deficiency

Iron is necessary for normal thyroid hormone synthesis because thyroid peroxidase is an iron-dependent enzyme. Iron deficiency may therefore contribute to impaired thyroid function and can coexist with Hashimoto's thyroiditis. Some evidence suggests an inverse relationship between iron status and the risk of autoimmune thyroid disease in women of reproductive age. One study reported that each unit increase in iron level was associated with a 43% reduction in the risk of Hashimoto's thyroiditis.[99] Patients with suspected iron deficiency should undergo appropriate laboratory assessment, including complete blood count, serum ferritin, and other iron studies when indicated. Identified deficiency should be treated according to its severity and underlying cause. Clinicians should also investigate possible contributors, such as inadequate dietary intake, gastrointestinal blood loss, celiac disease, and autoimmune atrophic gastritis. Iron supplements should be taken separately from levothyroxine to avoid reducing thyroid hormone absorption.

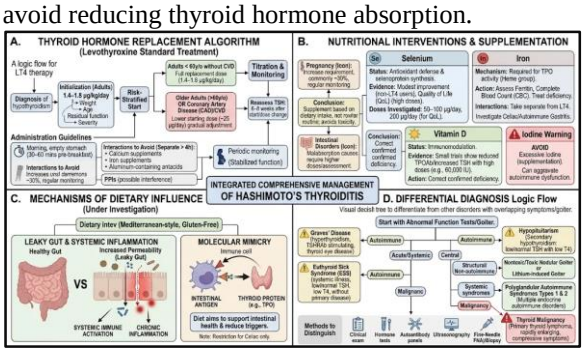


Figure-3: Comprehensive management and treatment lines of Hashimoto's Thyroiditis.

Vitamin D Deficiency Treatment

Vitamin D has immunomodulatory functions and may influence autoimmune activity. Vitamin D deficiency is frequently reported in individuals with autoimmune thyroid disorders, although its causal relationship with Hashimoto's thyroiditis remains uncertain. Correcting documented deficiency is appropriate for general health and may also provide benefits for thyroid-related outcomes. Small randomized clinical trials have reported reductions in thyroid antibody concentrations and improvements in TSH levels following vitamin D supplementation. An Indian trial administered cholecalciferol at 60,000 IU to participants over eight weeks and reported improvements in thyroid-related laboratory parameters.[100] A Chinese study compared daily cholecalciferol at 800 IU with the same supplementation combined with levothyroxine at 25–50 µg/day over six months.[101] Another study in Greece involving 186 vitamin D-deficient individuals reported a reduction in TPOAb levels following supplementation for four months.[102] A systematic review and meta-analysis involving 862 participants also identified beneficial effects on thyroid function and antibody concentrations.[103] Despite these findings, further large-scale studies are required to establish the clinical effectiveness of vitamin D supplementation specifically for Hashimoto's thyroiditis. Supplementation should primarily aim to correct confirmed deficiency, with dose selection guided by baseline vitamin D levels, patient characteristics, and clinical monitoring.

Dietary Modifications

Dietary interventions have received increasing attention in the management of autoimmune thyroid disorders. Proposed approaches include Mediterranean-style diets, gluten-free diets, and other anti-inflammatory dietary patterns. These interventions aim to improve nutritional status, support intestinal health, and reduce factors that may contribute to systemic inflammation. However, evidence supporting specific autoimmune diets remains limited, and no particular dietary pattern has been established as a standard treatment for Hashimoto's thyroiditis. One proposed mechanism involves increased intestinal permeability, sometimes described as leaky gut syndrome. This hypothesis suggests that disruption of the intestinal barrier may allow substances to cross the gut mucosa and stimulate immune responses. Molecular mimicry has also been proposed as a possible mechanism through which immune responses against intestinal antigens may cross-react with thyroid proteins, including thyroid peroxidase. However, these mechanisms remain under investigation and should not be considered established explanations for the disease. The autoimmune protocol diet is intended to support intestinal health and reduce exposure to foods thought to trigger inflammation, although its effectiveness has not been adequately established.[104] A small study involving 40 women reported improvements in thyroid function and reductions in TPOAb and TgAb concentrations following a Mediterranean, gluten-free dietary intervention.[105] These findings require confirmation in larger controlled trials. Gluten restriction is particularly relevant for patients with

confirmed celiac disease rather than being routinely recommended for all individuals with Hashimoto's thyroiditis. Overall, dietary management should emphasize a balanced intake of vegetables, fruits, whole grains, adequate protein, and essential micronutrients. Patients should avoid excessive iodine supplementation because high iodine intake may aggravate autoimmune thyroid dysfunction. Dietary changes should complement, rather than replace, prescribed thyroid hormone therapy and regular clinical monitoring.

Differential Diagnosis

The differential diagnosis of Hashimoto's thyroiditis includes several disorders that affect thyroid structure, hormone production, or immune function. Accurate differentiation is essential because these conditions may present with similar clinical findings, including goiter, fatigue, weight changes, and abnormal thyroid function tests. Graves' disease is an important differential diagnosis because it causes autoimmune hyperthyroidism and may present with diffuse thyroid enlargement and thyroid eye disease. Unlike Hashimoto's thyroiditis, it is commonly associated with stimulating TSH receptor antibodies. Euthyroid sick syndrome should also be considered in patients with abnormal thyroid hormone measurements during acute or chronic systemic illness, without primary thyroid disease. Hypopituitarism can produce secondary hypothyroidism characterized by low or normal TSH despite reduced circulating T4. Other structural and functional thyroid disorders include nontoxic goiter, toxic nodular goiter, and lithium-induced goiter. These conditions may cause thyroid enlargement or altered hormone production through mechanisms different from autoimmune thyroid destruction. Polyglandular autoimmune syndromes types 1 and 2 should be considered when thyroiditis occurs alongside other autoimmune endocrine disorders. Thyroid malignancies, particularly primary thyroid lymphoma, require consideration in patients with rapidly enlarging thyroid glands, persistent nodules, or compressive symptoms. Clinical examination, thyroid function tests, antibody measurements, ultrasonography, and, when indicated, fine-needle aspiration or biopsy help establish the diagnosis and distinguish Hashimoto's thyroiditis from these conditions.

Prognosis

The prognosis of Hashimoto's thyroiditis varies according to the degree of autoimmune thyroid damage, baseline thyroid function, antibody levels, age, and associated clinical conditions. Many individuals remain euthyroid for years and do not initially require thyroid hormone replacement. However, the presence of thyroid autoantibodies indicates an increased risk of progressive thyroid dysfunction and eventual hypothyroidism. The risk of developing overt hypothyroidism has been estimated to increase by approximately 5% annually, although the individual rate of progression varies according to clinical and laboratory characteristics.[106] Patients with elevated TSH, positive thyroid peroxidase antibodies, and a goiter may have a greater likelihood of developing progressive thyroid failure. Some patients may experience a transient thyrotoxic phase before developing hypothyroidism, while others remain clinically stable. For patients who develop hypothyroidism, levothyroxine replacement generally provides effective control of thyroid hormone deficiency. Appropriate treatment can relieve symptoms, restore normal biochemical thyroid function, and reduce the risk of complications associated with prolonged hormone deficiency. However, lifelong treatment and monitoring are often necessary because autoimmune destruction of thyroid tissue is usually irreversible. Annual thyroid function testing is recommended for individuals with Hashimoto's thyroiditis, particularly those who are initially euthyroid. More frequent assessment may be necessary when symptoms develop, TSH becomes abnormal, pregnancy occurs, or treatment doses change. Patient education and regular follow-up support early detection and effective long-term disease management.

Complications

Hashimoto's thyroiditis may cause complications through progressive thyroid tissue destruction, hormonal imbalance, and associated autoimmune activity. The most common long-term complication is hypothyroidism, which may produce fatigue, weight gain, cold intolerance, constipation, dry skin, hair loss, brittle nails, depression, impaired concentration, and menstrual irregularities. Untreated severe hypothyroidism can lead to serious systemic complications, including myxedema coma, although this is uncommon. Some patients experience transient hyperthyroidism, known as Hashitoxicosis, resulting from the release of stored thyroid hormones during follicular cell destruction. Thyroid enlargement and persistent inflammation may also contribute to nodules, swallowing difficulties, or other compressive symptoms. Thyroid eye disease can occur in a minority of patients. Reproductive complications include menstrual disturbances, impaired fertility, pregnancy loss, and postpartum thyroid dysfunction. Inadequate treatment during pregnancy may adversely affect maternal and fetal health. Conversely, excessive levothyroxine dosing can produce symptoms of thyrotoxicosis, highlighting the importance of individualized treatment and regular monitoring. The relationship between Hashimoto's thyroiditis and papillary thyroid carcinoma remains uncertain. Studies have reported conflicting findings regarding cancer risk and clinical outcomes.[107–109] However, chronic autoimmune thyroiditis is associated with an

increased risk of primary thyroid lymphoma, a rare malignancy accounting for approximately 0.5% to 5% of thyroid cancers.[110–113] Rapid thyroid enlargement, persistent neck masses, and compressive symptoms require prompt investigation.

Consultations

The management of Hashimoto's thyroiditis may require collaboration among several healthcare professionals to address thyroid dysfunction, associated conditions, treatment adherence, and potential complications. An endocrinologist provides specialized assessment and management, including interpretation of thyroid function tests, selection and adjustment of levothyroxine doses, and evaluation of thyroid enlargement or suspicious nodules. Primary care physicians and internists coordinate routine follow-up, assess general health, identify associated metabolic or autoimmune disorders, and arrange periodic laboratory investigations. They also monitor treatment effectiveness and refer patients for specialist assessment when symptoms persist or complications develop. Pharmacists contribute by educating patients about correct levothyroxine administration, medication interactions, and adherence. They should explain the importance of taking levothyroxine consistently on an empty stomach and separating it from calcium and iron supplements to avoid impaired absorption. Nurses support treatment through patient education, symptom assessment, medication review, monitoring, and reinforcement of follow-up schedules. Women experiencing infertility, recurrent pregnancy loss, or thyroid dysfunction during pregnancy may require consultation with obstetricians, reproductive endocrinologists, or fertility specialists. Pregnant patients need closer monitoring because thyroid hormone requirements may change during gestation. Ophthalmologists should assess patients with suspected thyroid eye disease, particularly those reporting visual changes, eye discomfort, or impaired eye movement. Additional referrals may be appropriate when patients have suspected celiac disease, nutritional deficiencies, or other autoimmune conditions. This coordinated approach promotes continuity of care, early identification of complications, appropriate treatment, and improved patient outcomes.

Conclusion:

Hashimoto's thyroiditis is a chronic autoimmune condition that can progressively impair thyroid function and lead to hypothyroidism. Its development involves genetic susceptibility, environmental influences, and immune-mediated destruction of thyroid tissue. Clinical presentation varies from an asymptomatic euthyroid state to overt hypothyroidism, making appropriate laboratory evaluation and long-term monitoring essential. Thyroid function tests, particularly TSH and T4, combined with thyroid autoantibody measurements, provide the basis for diagnosis. Levothyroxine remains the standard treatment for patients with hypothyroidism, while nutritional deficiencies and associated autoimmune conditions should be identified and managed when present. Regular follow-up helps assess treatment effectiveness, detect disease progression, and reduce complications. Nursing care plays an important role through symptom assessment, medication education, adherence support, and patient guidance regarding follow-up and lifestyle practices. A coordinated, patient-centered approach involving physicians, nurses, pharmacists, and relevant specialists can improve disease control, support reproductive and general health, and maintain quality of life.

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