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GENETIC AND IMMUNOLOGICAL PREDICTORS OF AUTOIMMUNE THYROIDITIS

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Abstract

Autoimmune thyroiditis (AIT) is one of the most common autoimmune endocrine disorders characterized by chronic inflammatory destruction of thyroid tissue mediated by genetic, immunological, and environmental factors. The disease develops due to complex interactions between immune dysregulation and genetic susceptibility, leading to progressive thyroid dysfunction. The aim of this study was to analyze the major genetic and immunological predictors associated with autoimmune thyroiditis and evaluate their role in early diagnosis and disease progression. The review demonstrated that specific genetic polymorphisms, including HLA genes, CTLA-4, PTPN22, and FOXP3, are significantly associated with increased susceptibility to autoimmune thyroid diseases. Immunological predictors such as elevated antithyroid antibodies, cytokine imbalance, T-cell dysregulation, and chronic inflammatory activation also play a central role in disease pathogenesis. Identification of these predictors may improve early diagnosis, risk stratification, and personalized therapeutic approaches in patients with autoimmune thyroiditis.

Keywords: autoimmune thyroiditis, Hashimoto thyroiditis, genetic predictors, immunological predictors, thyroid autoimmunity, cytokines, HLA genes, antithyroid antibodies.

Introduction

Autoimmune thyroiditis (AIT), commonly known as Hashimoto thyroiditis, is a chronic autoimmune disease characterized by lymphocytic infiltration and progressive destruction of thyroid tissue [1]. It represents one of the most prevalent autoimmune disorders worldwide and is considered the leading cause of hypothyroidism in iodine-sufficient regions [2].

The incidence of autoimmune thyroid diseases has increased significantly over recent decades, particularly among women [3]. Epidemiological studies indicate that genetic predisposition, environmental influences, hormonal factors, and immune dysregulation contribute to disease development [4]. Although the exact etiology remains incompletely understood, autoimmune thyroiditis is currently recognized as a multifactorial disorder involving complex interactions between inherited susceptibility and immune-mediated tissue damage [5].

Genetic factors play a fundamental role in autoimmune thyroiditis pathogenesis. Family aggregation studies demonstrate a higher prevalence of thyroid autoimmunity among first-degree relatives of affected individuals [6]. Twin studies further support the strong hereditary component of the disease [7]. Several susceptibility genes have been identified, including human leukocyte antigen (HLA) genes, cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4), protein tyrosine phosphatase non-receptor type 22 (PTPN22), FOXP3, and thyroglobulin-related genes [8].

The HLA system is one of the most extensively studied genetic factors associated with autoimmune thyroid diseases. Certain HLA-DR and HLA-DQ alleles are linked to increased risk of thyroid autoimmunity due to altered antigen presentation and immune tolerance mechanisms [9].

Similarly, CTLA-4 polymorphisms may impair T-cell regulation and contribute to autoimmune activation [10].

Immunological mechanisms are equally important in disease progression. Autoimmune thyroiditis is characterized by excessive activation of autoreactive T lymphocytes, B-cell stimulation, cytokine imbalance, and production of antithyroid antibodies [11]. Elevated serum levels of thyroid peroxidase antibodies (TPO-Ab) and thyroglobulin antibodies (Tg-Ab) are considered major immunological markers of disease activity [12].

Cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ), and interleukin-17 (IL-17) contribute to chronic inflammatory processes and thyroid tissue destruction [13]. Dysregulation of regulatory T cells (Tregs) and imbalance between Th1 and Th17 immune responses are also critically involved in autoimmune thyroid pathology [14].

Recent advances in molecular genetics and immunology have expanded understanding of predictive markers associated with autoimmune thyroiditis. Identification of genetic and immunological predictors may facilitate earlier diagnosis, assessment of disease severity, and development of individualized therapeutic strategies [15].

The purpose of this article was to analyze current evidence regarding the major genetic and immunological predictors of autoimmune thyroiditis and evaluate their pathogenetic and clinical significance.

Materials and Methods

This study was conducted as an analytical review of scientific literature dedicated to autoimmune thyroiditis and its genetic and immunological predictors. Scientific articles indexed in PubMed, Scopus, Web of Science, and Google Scholar databases were analyzed.

The inclusion criteria consisted of original clinical studies, genetic investigations, immunological analyses, systematic reviews, and meta-analyses related to autoimmune thyroid diseases.

The analyzed parameters included genetic polymorphisms, antithyroid antibody levels, cytokine profiles, T-cell dysregulation, inflammatory markers, and clinical manifestations associated with autoimmune thyroiditis.

Comparative and descriptive analytical methods were applied to evaluate the pathogenetic significance of identified predictors.

Results

The analysis demonstrated that autoimmune thyroiditis is strongly associated with both hereditary predisposition and immune system dysregulation. Several genetic polymorphisms showed statistically significant association with increased disease susceptibility.

Among genetic predictors, HLA-DR3, HLA-DR4, and HLA-DR5 alleles were most frequently associated with autoimmune thyroid diseases. CTLA-4 gene polymorphisms were linked to impaired immune tolerance and excessive autoreactive T-cell activation.

PTPN22 mutations were associated with abnormal lymphocyte signaling and increased autoimmune activity. FOXP3 abnormalities contributed to dysfunction of regulatory T cells and loss of immune suppression mechanisms.

Immunological evaluation revealed elevated serum concentrations of thyroid peroxidase antibodies and thyroglobulin antibodies in the majority of patients with autoimmune thyroiditis. Increased levels of proinflammatory cytokines, including IL-6, TNF-α, IFN-γ, and IL-17, were also observed.

The study demonstrated significant imbalance between proinflammatory and anti-inflammatory immune responses. Reduced regulatory T-cell activity and excessive Th1/Th17 immune activation contributed to chronic thyroid inflammation and progressive tissue destruction.

Patients with combined genetic susceptibility and elevated immunological markers showed more severe clinical progression and higher risk of hypothyroidism development.

Discussion

The findings confirm that autoimmune thyroiditis develops through complex interactions between genetic predisposition and immune-mediated inflammatory mechanisms. Genetic susceptibility alone is insufficient for disease manifestation; environmental and immunological triggers are also required for autoimmune activation.

The strong association between HLA alleles and autoimmune thyroiditis emphasizes the importance of antigen presentation pathways in disease pathogenesis. Altered immune recognition of thyroid antigens may initiate autoreactive T-cell responses and chronic inflammation.

CTLA-4 and PTPN22 polymorphisms further contribute to immune dysregulation by impairing normal inhibitory pathways responsible for maintaining self-tolerance. These findings support the concept that defective immune checkpoint regulation is central to autoimmune thyroid disease development.

The role of antithyroid antibodies remains particularly important in clinical practice. Elevated TPO-Ab and Tg-Ab levels not only serve as diagnostic markers but may also predict disease progression and thyroid functional impairment.

Cytokine imbalance and chronic inflammatory activation contribute directly to thyroid follicular destruction and fibrosis. Excessive Th1 and Th17 immune responses may amplify autoimmune reactions and perpetuate tissue damage.

Understanding genetic and immunological predictors may improve early identification of high-risk individuals before overt thyroid dysfunction develops. Personalized approaches based on molecular and immunological profiling may enhance disease prevention and treatment strategies.

Future research should focus on epigenetic regulation, microbiome interactions, and targeted immunomodulatory therapies for autoimmune thyroid diseases.

Conclusion

Autoimmune thyroiditis is a multifactorial endocrine disorder strongly associated with genetic susceptibility and immune system dysregulation. The disease develops through complex interactions involving hereditary factors, autoreactive immune responses, cytokine imbalance, and chronic inflammatory activation.

Genetic predictors such as HLA alleles, CTLA-4, PTPN22, and FOXP3 polymorphisms significantly contribute to increased risk of thyroid autoimmunity. Immunological markers, including elevated antithyroid antibodies and inflammatory cytokines, play essential roles in disease progression and thyroid tissue destruction.

Identification of genetic and immunological predictors may improve early diagnosis, prognostic assessment, and individualized therapeutic strategies in patients with autoimmune thyroiditis. Integrated molecular and immunological approaches may contribute to more effective prevention and personalized management of autoimmune thyroid diseases.

Further clinical and experimental investigations are required to clarify the pathogenetic mechanisms underlying thyroid autoimmunity and develop targeted therapeutic interventions.

References

1. Weetman AP. Autoimmune thyroid disease. *Autoimmunity.* 2004;37(4):337–340.
2. Caturegli P, et al. Hashimoto thyroiditis. *Lancet.* 2014;383:1555–1565.
3. Vanderpump MP. Epidemiology of thyroid disorders. *Br Med Bull.* 2011;99:39–51.
4. Antonelli A, et al. Autoimmune thyroid disorders. *Autoimmun Rev.* 2015;14:174–180.
5. Tomer Y, Huber A. The etiology of autoimmune thyroid disease. *Endocr Rev.* 2009;30:539–547.
6. Brix TH, et al. Genetic factors in autoimmune thyroid disease. *Clin Endocrinol.* 2001;55:363–368.
7. Hansen PS, et al. Twin studies in thyroid autoimmunity. *J Clin Endocrinol Metab.* 2006;91:731–736.
8. Ban Y, Tomer Y. Genetic susceptibility in autoimmune thyroid disease. *Mol Cell Endocrinol.* 2005;242:65–75.
9. Jacobson EM, et al. HLA associations in thyroid autoimmunity. *Thyroid.* 2008;18:667–674.
10. Kavvoura FK, et al. CTLA-4 gene polymorphisms. *J Clin Endocrinol Metab.* 2007;92:3162–3170.
11. Ajjan RA, Weetman AP. Immune mechanisms in thyroid autoimmunity. *Clin Exp Immunol.* 2015;181:183–191.
12. McLeod DS, Cooper DS. Thyroid antibodies and disease progression. *Lancet Diabetes Endocrinol.* 2012;1:123–131.
13. Figueroa-Vega N, et al. Cytokine profiles in autoimmune thyroiditis. *J Clin Endocrinol Metab.* 2010;95:953–962.
14. Bossowski A, et al. Regulatory T cells in autoimmune thyroid disease. *Mediators Inflamm.* 2013;2013:981–987.
15. Effraimidis G, Wiersinga WM. Clinical relevance of thyroid autoimmunity predictors. *Eur J Endocrinol.* 2014;170:R241–R252.