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Review Article
How Allergic Rhinitis Affects Thyroid Autoimmunity: A Systematic Evaluation and Meta-Analysis

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Abstract

Allergic rhinitis (AR), one of the most prevalent chronic conditions worldwide, results from immune system reactions to inhaled allergens mediated by the Immunoglobulin E (IgE) molecule. While individual symptoms may appear harmless, their collective impact can significantly diminish an individual's overall quality of life. Moreover, AR's repercussions extend beyond the observable symptoms, as it frequently coexists with various health disorders, including asthma. Allergic rhinitis is classified into two distinct categories: Local allergic rhinitis and occupational rhinitis, both characterized by typical allergic responses. Thyroid autoimmunity encompasses a range the thyroid issues triggered when the immune system, the body's primary defense mechanism, is activated. Conditions such as Hashimoto's thyroiditis and Graves' disease exemplify thyroid autoimmune diseases. Studies indicate a less common mechanism differentiating thyroid autoimmunity from allergic rhinitis. Specifically, thyroid autoimmunity is associated with a Th1-dominated immune response, while allergic rhinitis is linked to a Th2-dominated immunological response. Nevertheless, they share some distinct traits, including a shared genetic predisposition, immune system dysregulation and exposure to environmental triggers. Chronic inflammation induced by allergic rhinitis may regulate exacerbated autoimmune responses, but further investigation is needed to substantiate these findings.

Key words: Allergy rhinitis, Grave's disease, Hashimoto's thyroiditis, thyroid autoimmunity, meta-analysis

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Allergic rhinitis (AR) is a common chronic condition characterized by inflammation of the nasal passages due to an immune system response to inhaled allergens. The AR stands out as one of the most prevalent and persistent medical conditions globally, stemming from Immunoglobulin E (IgE)-mediated reactions to inhaled allergens[1]. Given its substantial impact on a significant portion of the global population, AR is a widespread allergic disorder of considerable importance. Notable symptoms distinguishing this condition include chronic sneezing, nasal pruritus, congestion and rhinorrhea[2]. Occupational rhinitis, an inflammatory nasal condition, is characterized by intermittent or recurring symptoms like restricted airflow, excessive nasal secretion, sneezing and itching, often linked to specific work environments. Importantly, there is currently no evidence supporting the progression of occupational rhinitis to occupational asthma with prolonged exposure[3].

In the absence of systemic atopy, local allergic rhinitis (LAR) presents itself as a clinical condition marked by a localized allergic response in the nasal mucosa. While the outcomes of treating LAR remain uncertain, there is some evidence suggesting that allergen immunotherapy might prove beneficial in addressing this specific type of rhinitis[4]. The frequent occurrence of thyroid autoimmunity, coupled with the thyroid gland's crucial involvement in numerous metabolic processes, designates it as a significant autoimmune disorder[5]. Situated at the base of the neck, this small yet vital organ becomes a target of the immune response due to its misdirected focus. Often likened to a butterfly in structure, the thyroid gland plays a pivotal role in producing hormones that regulate various metabolic processes[6].

Autoimmune disorders encompass a collection of diseases wherein the body's immune system mounts an excessive response against its own cells, tissues and organs, leading to inflammation and damage[7]. Hashimoto's thyroiditis (HT) ranks as the most prevalent autoimmune thyroid disease, affecting approximately 20-30% of individuals, with a higher incidence in females than males. Other contributing factors to this condition include age, gender and geographic variations[8]. For the management of Hashimoto's thyroiditis, treatments such as Levothyroxine (LT4) and selenium (Se) supplementation may demonstrate effectiveness. Graves' disease, on the other hand, is characterized by autoimmune reactions caused by antibodies to the thyrotropin receptor, resulting in hyperactivity of the thyroid gland[9]. Tailoring treatment approaches based on individual patient preferences and specific clinical characteristics, including age, history of ischemic heart disease or arrhythmia, goiter size and severity of thyrotoxicosis, is crucial. Physicians must be well-versed in the advantages and disadvantages of various therapies to provide optimal and effective care for their patients[10].

A growing body of research suggests a potential link between thyroid autoimmunity, specifically Hashimoto's thyroiditis and allergic rhinitis. Some studies propose that individuals with allergic rhinitis exhibit a higher prevalence of thyroid autoimmunity, suggesting a potential correlation between immune dysregulation and susceptibility to both conditions[11]. From an immunological perspective, autoimmune thyroid disorders are linked to a Th1-dominant immune response, while allergic rhinitis is commonly associated with a Th2-dominated immune response. This highlights a complex interplay between immune system pathways, providing insights into the potential shared mechanisms or triggers that contribute to the co-occurrence of these disorders[12].

In recent years, there has been a growing interest in understanding the intricate connections between various immune-related disorders. One intriguing area of exploration revolves around the potential interplay between allergic rhinitis and thyroid autoimmunity, particularly in the context of Hashimoto's thyroiditis. This systematic evaluation and meta-analysis aim to shed light on the relationship between allergic rhinitis and thyroid autoimmunity by synthesizing existing research findings. As the prevalence of both conditions continues to rise globally, unraveling the immunological nuances that link them may offer valuable insights into shared mechanisms and therapeutic implications. Through a comprehensive examination of the available literature, this study seeks to contribute to a deeper understanding of how allergic rhinitis influences thyroid autoimmunity, potentially paving the way for more targeted and effective interventions in the realm of autoimmune and allergic disorders.

METHODOLOGY

Data was searched from websites Sci Hub, Google Scholar and PubMed by typing words "Allergy rhinitis" and "Thyroid autoimmunity" separately. There were 5057 articles after inclusion criteria (research and review with full length), only 48 articles were included in this study (Fig. 1).

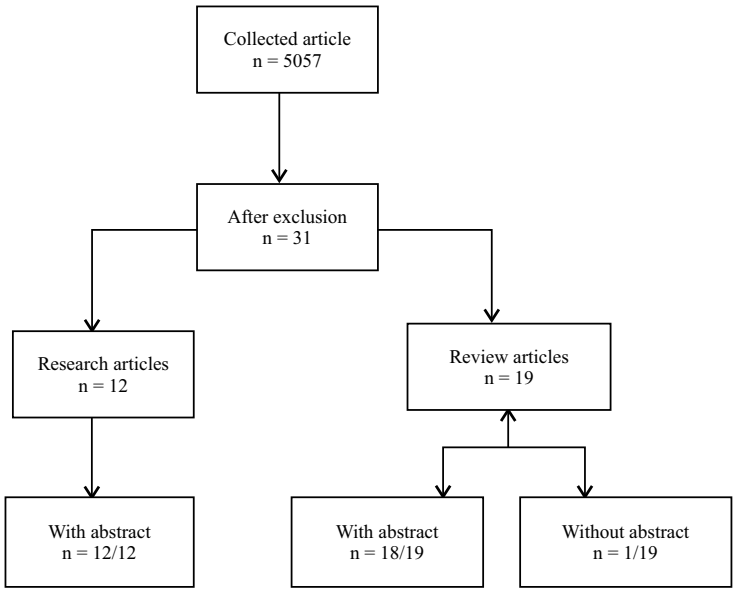

Fig. 1: Flow diagram shows the process of identifying and including datasets for random effect meta-analysis

Allergic rhinitis: The allergic rhinitis (AR) ranks among the prevalent and persistent global medical conditions, resulting from immune responses mediated by Immunoglobulin E (IgE) to allergens inhaled by individuals[13]. The AR, a common and widespread allergic condition, is significant because it affects a large portion of the global population[14]. The AR, which manifests largely as an excessive immune reaction to airborne allergens, initiates a cascade of inflammatory responses that are primarily localised within the nasal airways[15]. This medical condition is distinguished by a number of bothersome symptoms, including but not limited to chronic sneezing, nasal pruritus, congestion and rhinorrhoea[16]. Each symptom, while seemingly benign in isolation, converges to generate a condition that can considerably damage an individual's overall quality of life. Furthermore, the reach of AR extends beyond these direct symptoms, as it overlaps with numerous health issues, one such example being asthma[17]. The widespread prevalence of AR needs a thorough understanding of the disorder, as its consequences extend far beyond the core symptoms. As a result, investigating AR's possible influence on other health issues becomes critical. The majority of therapy for the disease is second-generation oral antihistamines and intranasal corticosteroids. Under specific conditions, allergen immunotherapy, along with supplementary medications like decongestants and oral corticosteroids, may prove advantageous (Fig. 2)[18].

Occupational rhinitis: The occupational rhinitis presents as an inflammatory nasal condition featuring intermittent or persistent symptoms like restricted airflow, excessive secretion, sneezing and itching. These symptoms are triggered by a specific occupational environment rather than external stimuli[19]. Though the exact prevalence of occupational rhinitis is not well-established, occupations with elevated risks include those in farming, veterinary work, laboratory or food processing and various commercial industries[20]. The mainstay of treatment involves avoiding exposure to the causative agent, and, when necessary, utilizing medications. Prolonged exposure indicates limited evidence of occupational rhinitis progressing to occupational asthma[21].

Local allergic rhinitis: The local allergic rhinitis (LAR) is a clinical condition marked by a specific allergic reaction in the nasal mucosa, occurring without systemic atopy[22]. The symptoms of LAR resemble those of allergic rhinitis and there is an assumption that LAR is an IgE-mediated condition, supported by clinical observations and the identification of specific IgE in the nasal mucosa[23]. The results of treating LAR remain uncertain, although certain data suggests that allergen immunotherapy may be advantageous for managing this form of rhinitis[24].

Thyroid autoimmunity: The thyroid autoimmunity is a serious autoimmune condition due to its frequency and the thyroid gland's vital participation in various metabolic activities[25,26]. Thyroid autoimmunity is a group of diseases that occur when the body's immune system, which normally serves as a defense mechanism against outside infections, begins to

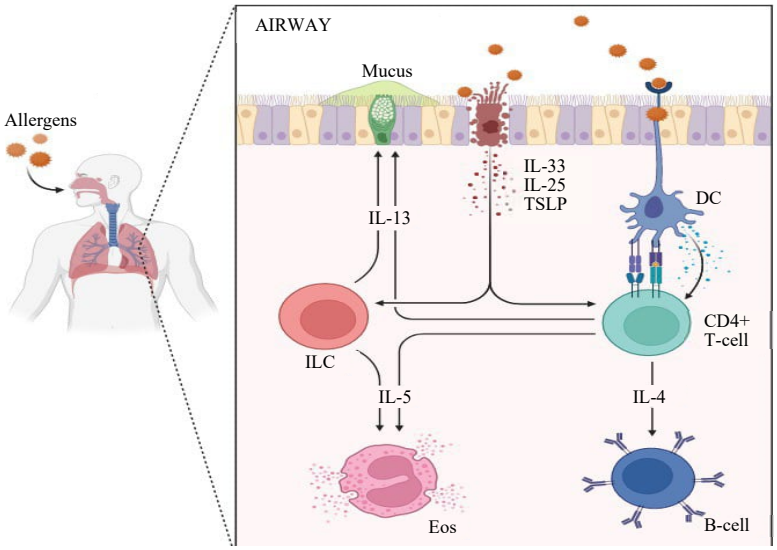

Fig. 2: Immunological mechanism of an allergic rhinitis

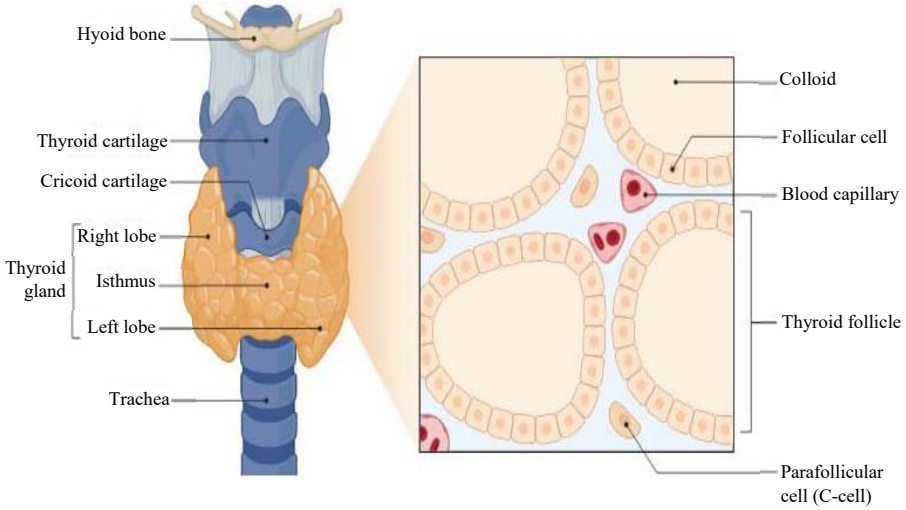

Fig. 3: Anatomy of thyroid gland

mistakenly recognize the thyroid gland as a threat[27]. This misdirected immune response leads to an attack on the thyroid gland, a small but vital organ located at the base of the neck.

The thyroid gland (Fig. 3), often likened to a butterfly due to its shape, is a central organ of the body's metabolism. It is responsible for the production of hormones that regulate various metabolic processes, influencing everything from heart rate and body temperature to the conversion of food into energy[28].

Autoimmune thyroid disease: The autoimmune disorders are a group of diseases in which the body's immune system overreacts against its own cells, tissues and organs, causing inflammation and damage[25]. The primary forms of thyroid autoimmunity include Hashimoto's thyroiditis and Graves' disease[29]. Hashimoto's thyroiditis, named after the Japanese physician Hakaru Hashimoto who first described it, is characterized by a gradual failure of the thyroid gland due to a persistent autoimmune attack. This often leads to hypothyroidism, a condition in which the thyroid gland is underactive and does not produce enough thyroid hormones, leading to a slowdown of metabolic processes[30]. On the other end of the spectrum is Graves' disease, which can result in hyperthyroidism, a condition where the thyroid gland is overactive. In this scenario, excess thyroid hormones are

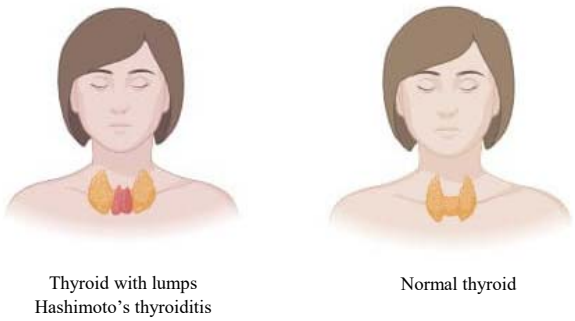

Fig. 4: Visual representation of Hashimoto's disease

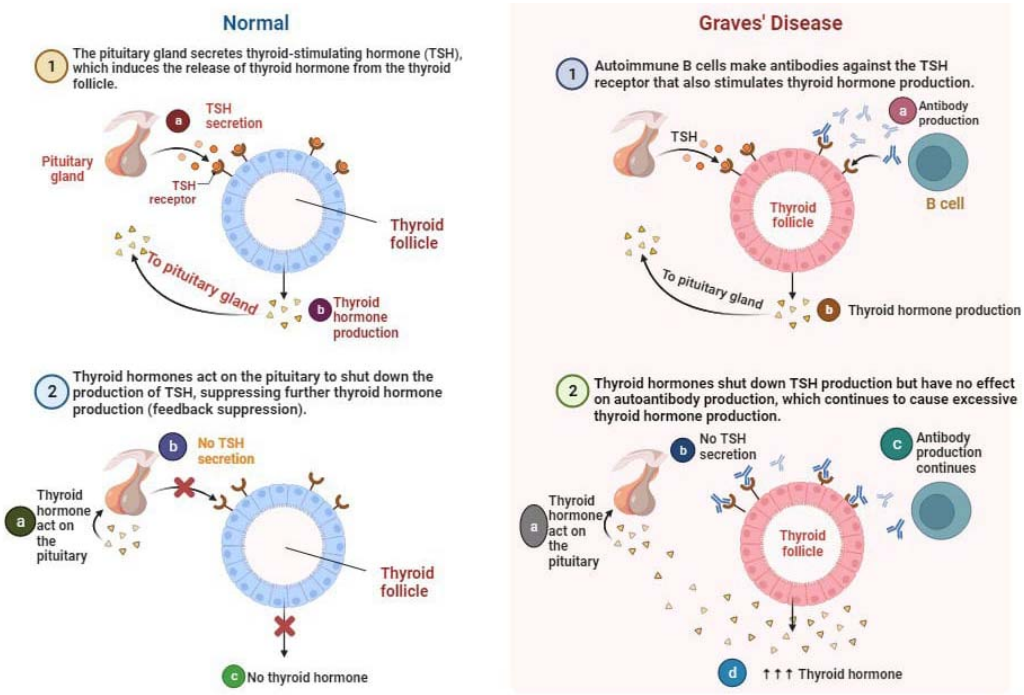

Fig. 5: Mechanism of Grave's disease

produced, accelerating the body's metabolism, which can manifest in symptoms such as rapid heart rate, weight loss and nervousness[31].

The significant health implications associated with both conditions necessitate a comprehensive understanding of their triggers and influences. Unveiling these aspects could provide valuable insights for early detection, prevention strategies and the development of more effective therapeutic interventions. It is this context that makes the exploration of potential links between these conditions and other health disorders a topic of considerable interest in contemporary medical research.

Hashimoto's thyroiditis: Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid diseases. About 20-30% of individuals develop hypothyroidism as a result of the persistent inflammation of the thyroid tissue that it produces (Fig. 4)[32]. Epidemiological studies have uncovered several key findings: (i) The risk of autoimmune thyroiditis (AIT) is greater in women compared to men, (ii) AIT hypothyroidism exhibits an age-related pattern, (iii) There is geographical heterogeneity, (iv) The incidence of AIT is higher in iodine-sufficient conditions compared to iodine-deficient conditions and (v) The prevalence of antithyroid antibodies (ATA) varies among different races, increases with age and decreases with smoking[33]. Thyroid dysfunction and thyroiditis can be identified by AbTPO. About 80-90% of those diagnosed with AIT have circulating AbTPO[33]. There is evidence that levothyroxine (LT4) and selenium (Se) supplementation may be effective in treating Hashimoto's thyroiditis (HT)[34].

Graves' diseases: Graves' disease is an autoimmune disease in which the thyroid is activated by antibodies to the thyrotropin receptor. One of the numerous physical and psychological symptoms of a medical condition that might reduce life expectancy and quality is the hyperthyroidism that develops[31]. Treatment options for Grave's disease include thyroid surgery, RAI and antithyroid medication (Fig. 5). The best course of action is determined by the patient's preferences and specific clinical features, including age, a history of ischemic heart disease or an arrhythmia, the size of the goiter and the severity of the thyrotoxicosis. To provide their patients with the most effective treatment, doctors should be informed about the benefits and drawbacks of each therapy[35].

INTERSECTION OF ALLERGIC RHINITIS AND THYROID AUTOIMMUNE

There is emerging evidence suggesting a potential relationship between allergic rhinitis and thyroid autoimmunity, particularly Hashimoto's thyroiditis[36]. Some studies have found a higher prevalence of thyroid autoimmunity in individuals with allergic rhinitis, suggesting a possible link between immune dysregulation and susceptibility to both conditions[37]. However, the exact mechanisms underlying this connection are not fully understood. Possible factors that could contribute to this intersection include shared genetic susceptibility, immune system dysregulation and environmental triggers. Chronic inflammation associated with allergic rhinitis might play a role in triggering or exacerbating autoimmune responses, although more research is needed to confirm these hypotheses.

POTENTIAL LINKS BETWEEN ALLERGIC RHINITIS AND THYROID AUTOIMMUNITY

Allergic rhinitis and thyroid autoimmunity are both common immune-related conditions that can coexist in some individuals. While they are distinct conditions, there is emerging evidence suggesting potential links between them, although the exact nature of these links is still not fully understood. Here are some potential connections and considerations.

Immunological cross-talk: Both allergic rhinitis and thyroid autoimmunity involve immune system dysregulation. Allergic rhinitis is characterized by an inappropriate immune response to allergens, leading to symptoms such as sneezing, nasal congestion and itching[38]. Thyroid autoimmunity, on the other hand, involves the immune system attacking the thyroid gland, resulting in conditions like Hashimoto's thyroiditis and Graves' disease[39]. According to Sakaguchi *et al.*[40], immune system's activity in one condition could potentially influence the development or severity of the other.

Shared genetic predisposition: Genetic factors play a role in the development of both allergic rhinitis and thyroid autoimmunity. Studies have identified certain genetic markers that are associated with an increased risk for both conditions. Shared genetic predisposition could contribute to the co-occurrence of these conditions in some individuals[41].

Inflammation and cytokines: Both conditions involve inflammation and the release of various cytokines, which are signalling molecules that regulate immune responses. Chronic inflammation in allergic rhinitis and autoimmune thyroid disorders could potentially influence each other's progression or exacerbation[42].

Th2 and Th1 imbalance: Allergic rhinitis is often associated with a Th2-dominated immune response, while autoimmune thyroid disorders are linked to a Th1-dominant response[43]. Imbalances between these immune responses could potentially contribute to the development or exacerbation of both conditions[40].

Environmental factors: Environmental factors, such as exposure to allergens, pollutants and infectious agents, can influence the immune system's behaviour and may play a role in the development of both conditions. These environmental triggers could potentially interact and contribute to the co-occurrence of allergic rhinitis and thyroid autoimmunity[44].

Hormonal influences: Hormones, especially sex hormones, are known to influence immune responses[45]. Thyroid autoimmunity is more common in females and hormonal changes during puberty, pregnancy and menopause can impact both thyroid function and immune responses. These hormonal fluctuations could potentially affect the development or severity of allergic rhinitis as well[46].

Autoimmune cascade: Some researchers propose the concept of an "autoimmune cascade," where the development of one autoimmune condition could trigger the development of others. This cascade could be driven by shared underlying immune dysregulation[47].

IMPLICATIONS: LOOKING BEYOND THE STUDY

The final phase of this review process involves a thorough examination of the study's implications. This encompasses an assessment of how the findings may impact our comprehension of allergic rhinitis and thyroid autoimmunity, their potential influence on future research avenues and their capacity to shape clinical practices[48]. The study under consideration, delving into the convergence of allergic rhinitis and thyroid autoimmunity, holds significant promise for steering future investigations in this domain. Should subsequent studies corroborate these findings, it has the potential to revolutionize our understanding of autoimmune thyroid disorders, potentially revealing novel therapeutic targets. On a clinical front, this connection could prompt a reevaluation of how patients with allergic rhinitis are managed, urging clinicians to maintain a closer vigil for signs of thyroid autoimmunity. This heightened awareness could lead to earlier detection and intervention, thereby enhancing patient outcomes. Nevertheless, it's crucial to contextualize the implications of a singular study within the broader literature landscape. Further research is imperative to validate these findings and gain a comprehensive understanding of the mechanisms underpinning the suggested link between allergic rhinitis and thyroid autoimmunity.

CONCLUSION

This review offers a comprehensive and in-depth analysis of "how allergic rhinitis affects thyroid autoimmunity". The exploration of the study's methodology, findings and potential implications positions it as a valuable resource for researchers and clinicians specializing in autoimmunity and allergies. The ongoing investigation in this field holds the promise of advancing our understanding of both allergic rhinitis and thyroid autoimmunity. This, in turn, has the potential to pave the way for enhanced diagnostic strategies, more precisely targeted therapeutic interventions and ultimately, improved patient outcomes. Extensive literature searches suggest that allergic rhinitis (AR) is a prevalent chronic disorder globally, resulting from immune system reactions to inhaled allergens through the Immunoglobulin E (IgE) molecule. While individual symptoms may appear benign, their cumulative impact forms a condition with the potential to significantly diminish a person's overall quality of life. Moreover, as AR frequently coexists with various health conditions, including asthma, its implications extend beyond the observable symptoms. Allergic rhinitis is categorized into two types: Occupational rhinitis, affecting the nose and local allergic rhinitis, characterized by a typical allergic reaction. Thyroid autoimmunity comprises a group of disorders affecting the thyroid gland, a central organ in the body. This occurs when the immune system, a crucial line of defense, perceives a thyroid function as a threat. Disorders such as Hashimoto's thyroiditis and Graves' disease fall under thyroid autoimmune disorders. Research indicates a less common mechanism linking allergic rhinitis and thyroid autoimmunity, where allergic rhinitis is associated with a Th2-dominated immune response, while thyroid autoimmunity is linked to a Th1-dominated immune response. Despite these differences, there are shared factors like genetic susceptibility, immune system dysregulation and environmental triggers. Chronic inflammation associated with allergic rhinitis may play a role in regulating autoimmune responses, but further research is needed to confirm these findings.

SIGNIFICANCE STATEMENT

The primary aim of this study was to articulate the necessity of our research and delineate the distinctive contributions it made to the academic discourse surrounding the article "how allergic rhinitis affects thyroid autoimmunity: A systematic evaluation and meta-analysis". Our objective was to underscore the relevance and imperative nature of our investigation, elucidating the unique insights and advancements it brought to the broader understanding of the interplay between allergic rhinitis and thyroid autoimmunity. Through a systematic evaluation and meta-analysis, our research aimed to provide nuanced perspectives, filling critical gaps in the existing literature and offering a substantial contribution to the ongoing academic dialogue in this field.

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