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# **PhD THESIS**

**CLINICAL AND EXPERIMENTAL STUDIES ON CHRONIC  
ALLERGIC RHINITIS**

Scientific coordinator

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The research project is part of the doctoral thesis of the student Dr. Andreea Iordache under the supervision of the doctoral coordinator Prof. Dr. Nicolae Balica from the Department IX of Surgery at the "Victor Babeș" University of Medicine and Pharmacy in Timișoara. The project aims to strengthen the link between chronic allergic rhinitis and certain pathologies (allergic conjunctivitis and bronchial asthma) and to identify cases of chronic allergic rhinitis with potential progression towards lesions of uncertain character. It seeks to raise awareness, develop effective prevention and treatment strategies, and improve public health by understanding their epidemiology, pathophysiology, and management.

The exploration of allergic rhinoconjunctivitis, a prevalent condition affecting millions worldwide, has been a focal point in medical history dating back to ancient civilizations. From early Egyptian remedies to modern pharmacological interventions, the journey of understanding and treating this ailment has been one of continuous advancement and adaptation. In this essay, we delve into the significance of studying allergic rhinoconjunctivitis, its impact on patients' lives, and the avenues it opens for medical innovation.

The repercussions of allergic rhinoconjunctivitis extend far beyond physiological discomfort, significantly impairing patients' quality of life. Symptoms ranging from nasal itching to ocular irritation impose daily hindrances, disrupting sleep patterns and inducing stress and anxiety. The resultant decrease in productivity and academic performance underscores the profound socio-economic ramifications of this condition. Furthermore, the emotional toll of chronic symptoms underscores the urgency of innovative therapeutic approaches to alleviate suffering and enhance well-being.

**Allergic rhinitis (AR)** is a prevalent condition affecting individuals worldwide, with reported occurrence ranging from 2% to over 40% across different age groups and regions. Recent epidemiological studies indicate a progressive increase in AR prevalence, particularly in Western societies, underscoring its significant impact on public health. Sensitization to allergens such as pollen and house dust mites plays a central role in AR pathogenesis, triggering immune responses and inflammatory processes in the nasal mucosa. The classification of AR based on symptom duration and severity guides treatment strategies, which encompass both non-pharmacological and pharmacological approaches. Non-pharmacological interventions include allergen avoidance, while pharmacological options range from H1 antihistamines and intranasal corticosteroids to leukotriene antagonists and allergen-specific immunotherapy (AIT). AIT, administered under specialist supervision, aims

to induce tolerance to allergens and alleviate symptoms in patients with persistent or uncontrolled AR. Understanding the epidemiology and pathophysiology of AR is crucial for optimizing management strategies and improving the quality of life for affected individuals

**Allergic conjunctivitis** is triggered by allergens like pollen, presents with symptoms such as itching and tearing. Diagnosis involves clinical evaluation and allergy tests. Prevalence varies globally, with increasing trends observed, especially in industrialized countries and Asia. The pathophysiology of allergic conjunctivitis involves IgE-mediated mast cell activation, leading to acute and late-phase allergic responses. Chronic inflammation may impact vision, with tear film inflammation contributing to ocular surface disorders.

**Allergic asthma** is the most common form of asthma, characterized by inflammation of the respiratory pathways due to sensitization to aeroallergens. It typically starts in childhood and is often linked with other allergic conditions. Diagnosis involves evaluating symptoms, pulmonary function tests, allergy assessments, and biomarker measurements. Prevalence varies globally but is increasing, with significant comorbidity with conditions like allergic rhinitis. The pathophysiology involves type TH2 immune reactions, driven by cytokines like IL-4, IL-5, and IL-13, and involving inflammatory cells such as mast cells and T cells.

**In short, the main objectives were:**

The main objectives of this research have been succinctly expressed and can be detailed as follows:

**1. Relationship between allergic rhinitis and allergic conjunctivitis (allergic rhinoconjunctivitis) - review:**

- Explore the literature to highlight the evolution of research regarding the relationship between allergic rhinitis and allergic conjunctivitis.
- Synthesize and present conclusions from relevant studies regarding the prevalence, common pathophysiological mechanisms, and therapeutic options for allergic rhinoconjunctivitis.

**2. A Review Regarding the Connections between Allergic Rhinitis and Asthma - Epidemiology, Diagnosis, and Treatment:**

- Investigate the epidemiology to highlight the predominance and frequency between allergic rhinitis and bronchial asthma.

- Examine the diagnostic methods of both conditions and evaluate current treatment modalities.
- Identify the pathophysiological connections and potential directions for improving the concurrent management of these two conditions.

### **3. Allergic rhinitis associated with nasal polyps and rhinosinusitis – histopathological and immunohistochemical study:**

- Conduct a detailed histopathological study to analyze tissue changes observed in the pathology of allergic rhinitis associated with nasal polyps and/or rhinosinusitis.
- Perform an immunohistochemical analysis to identify specific markers and highlight local immune changes in the context of allergic rhinitis associated with nasal polyps and/or rhinosinusitis.
- Compare the obtained results with existing literature to consolidate current knowledge and contribute to the development of new perspectives in researching this complex subject.

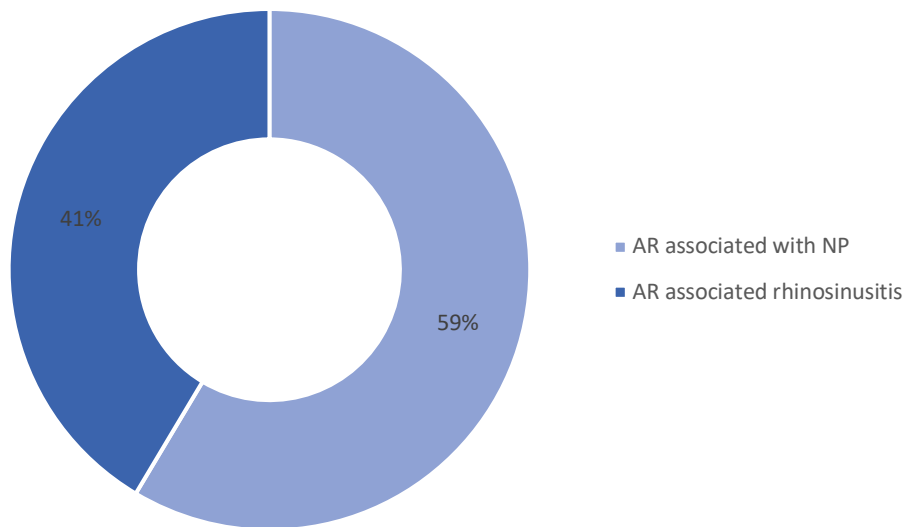
## **MATERIALS AND METHODS:**

The retrospective study analyzed patients admitted to the ENT Clinic of the Municipal Emergency Hospital, Timișoara, from 2016 to 2020, focusing on allergic rhinitis associated with nasal polyps and rhinosinusitis. Data included patient demographics, clinical and biological aspects, and histopathological diagnoses. Diagnostic methods involved comprehensive ENT examinations, including rhinoscopy and nasal endoscopy, along with symptom evaluation and diagnostic tests for allergic rhinitis and conjunctivitis.

## **RESULTS:**

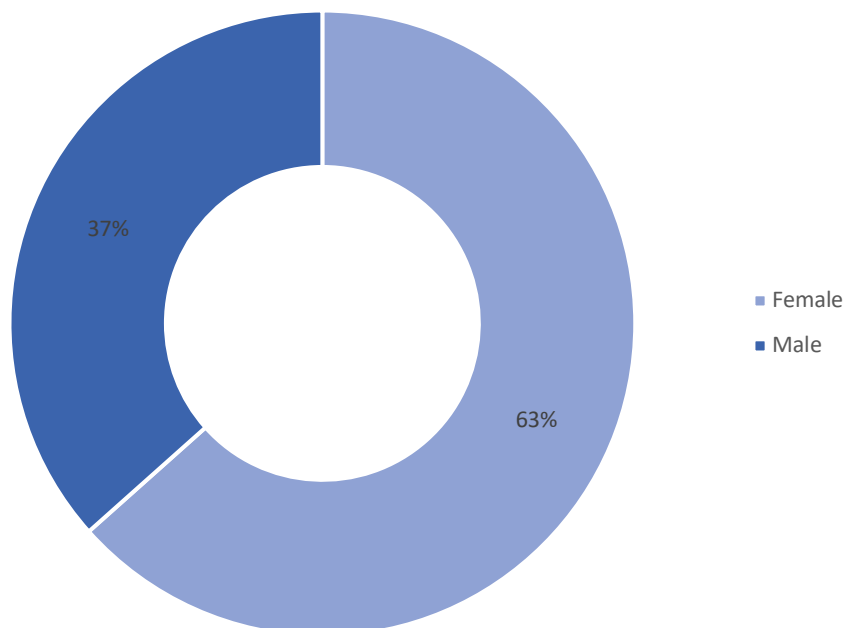
### **1. Patient Distribution:**

- Among patients admitted for nasal pathology, 70 were selected for the study.
- 41 (58.57%) had AR with NP, and 29 (41.42%) had AR with rhinosinusitis.



## 2. Demographics:

- AR with NP: 26 (63.41%) female, 15 (36.58%) male, 68% reported sleep disturbances.
- AR with Sinusitis: 14 (48.27%) female, 15 (51.2%) male, 59% reported sleep disorders.
- 58% urban, 42% rural patients indicated possibly easier access to urban healthcare.



### 3. Allergen Sensitivity:

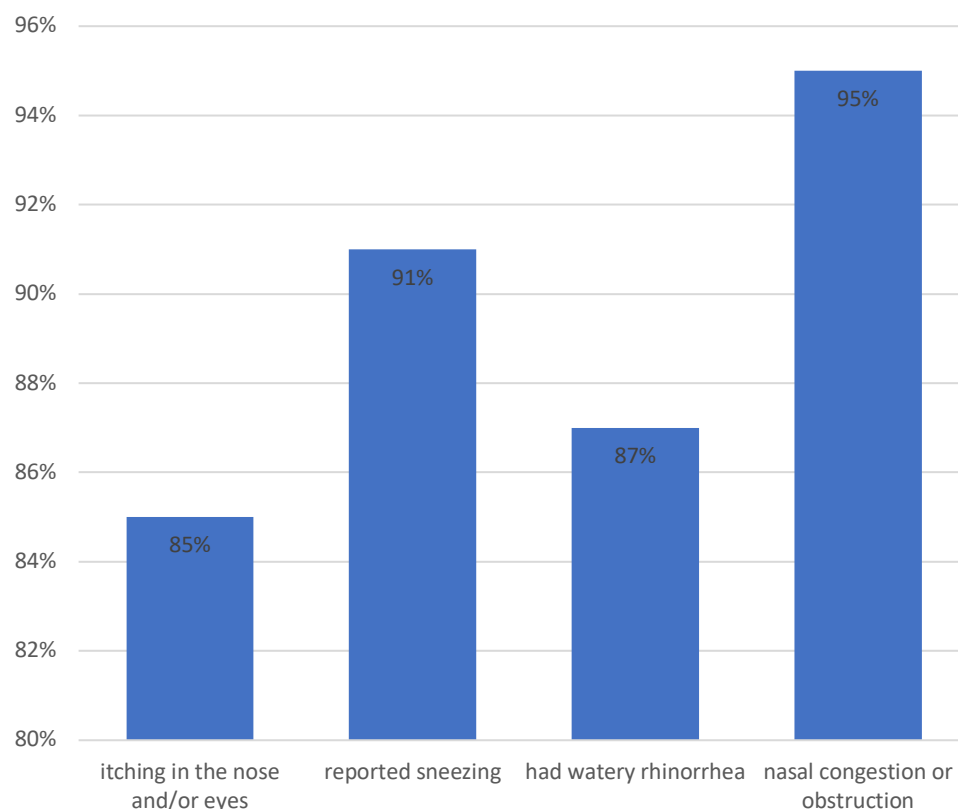
- Predominantly pollen allergies (75%), followed by indoor allergens: dust mites (55%), pets (43%), certain molds (49%).

### 4. Age Distribution:

- NP patients mostly middle-aged (average ~45 years), AR with NP group younger (average 34 years) than AR with sinusitis (average 39 years).

### 5. Symptoms:

- Predominant symptoms: nasal/ocular itching (85%), sneezing (91%), watery rhinorrhea (87%), nasal congestion/obstruction (95%).



### 6. Histopathological Findings:

- Rhinosinusal mucosa exhibited heterogeneous alterations: cilia reduction, intercellular space widening, goblet cell reduction, basal membrane thickening, necrosis.

- Chronic inflammatory process primarily characterized by eosinophils, lymphocytes, plasma cells, mast cells, and macrophages.

- Well-developed blood vascular network and fibroblast proliferation noted in some instances.

- B-lymphocytes infiltration estimated as minimal to moderate, T-lymphocytes predominantly detected in both lamina and surface epithelial cells.

These findings shed light on the complex pathological mechanisms underlying AR associated with NP and rhinosinusitis, emphasizing the need for comprehensive management strategies targeting both allergic and inflammatory components.

## **CONCLUSIONS:**

Interdependence and the importance of properly investigating and managing allergic rhinitis and associated conditions provide a comprehensive perspective on the relationship between these conditions and the necessity for medical personnel to be involved in the proper treatment and care of patients with this pathology.

**Epidemiological analysis, diagnosis, and treatment associated with allergic rhinitis and bronchial asthma have highlighted a significant interdependence between these two respiratory conditions.** The increased prevalence of asthma in patients with allergic rhinitis, as well as vice versa, emphasizes a close connection between these two pathological entities. Recognizing the common symptoms and risk factors of both conditions is essential for early diagnosis and proper management. A review of available therapies has highlighted the benefits of an integrated approach aiming to alleviate symptoms and reduce inflammation in both the upper and lower respiratory tracts.

**Investigating the distinctive changes** in nasal tissues and local inflammation associated with allergic rhinitis, nasal polyps, chronic rhinosinusitis, and sinonasal tumors **has contributed to understanding the pathogenic mechanisms and identifying new therapeutic possibilities.** Detailed analysis of tissue fragments has revealed the presence of specific markers of allergic inflammation and has identified morphological and immunological characteristics specific to these associated conditions, thus providing new perspectives for the efficient management of these complex clinical conditions.

**Histopathological study sheds light on the significant changes observed in the sinonasal mucosa in patients with allergic rhinitis (AR).** Microscopic analysis reveals profound changes in the structure and function of the mucosa, providing a clearer understanding of the pathophysiology of this condition.

Looking for specific signs in chronic rhinosinusitis has shown us that there's no one-size-fits-all approach to treatment. Finding the right treatment for each person's specific situation can make a big difference in their quality of life.