Case Report

Autonomic dysfunction in allergic rhinitis assessed by heart rate variability

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ABSTRACT

Background: Allergic rhinitis is a chronic inflammatory condition of the nose mediated by IgE, characterized by symptoms such as nasal congestion, rhinorrhea, repeated sneezing, and nasal itching. Autonomic nervous system dysfunction is a significant factor in the pathophysiology of allergic rhinitis. **Purpose:** To evaluate autonomic nervous system dysfunction in allergic rhinitis patients using heart rate variability. **Case report:** A 28-year-old woman with allergic rhinitis who underwent heart rate variability testing, revealed increased parasympathetic nervous system activity. **Method:** The study involved a literature search through PubMed, EBSCO, Scopus, and ScienceDirect, with screening based on inclusion and exclusion criteria. The selected literatures were critically reviewed using the Oxford Centre for Evidence-based Medicine's criteria for Etiology Studies. **Result:** Two cross-sectional studies were identified that matched the case report's PICO and eligibility criteria. Those studies showed patterns of autonomic nervous system dysfunction, marked by increased parasympathetic and decreased sympathetic activity in allergic rhinitis patients. **Conclusion:** The findings suggested that autonomic nervous system dysfunction played a role in the pathophysiology of allergic rhinitis, as evidenced by changes in heart rate variability.

Keywords: autonomic dysfunction, allergic rhinitis, heart rate variability

ABSTRAK

Latar belakang: *Rinitis alergi adalah suatu kondisi inflamasi kronis pada hidung yang dimediasi oleh IgE, ditandai dengan gejala berupa kongesti nasal (hidung tersumbat), rinore (keluarnya cairan dari hidung), bersin berulang, dan gatal pada hidung. Disfungsi sistem saraf otonom merupakan faktor penting dalam patofisiologi rinitis alergi.* ***Tujuan:*** *Untuk mengevaluasi disfungsi sistem saraf otonom pada pasien rinitis alergi dengan menggunakan variabilitas denyut jantung (*heart rate variability, HRV*).* ***Laporan kasus:*** *Seorang wanita usia 28 tahun dengan rinitis alergi menjalani pemeriksaan heart rate variability (HRV), yang menunjukkan peningkatan aktivitas sistem saraf parasimpatis.* ***Metode:*** *Penelitian ini melibatkan pencarian literatur melalui* PubMed, EBSCO, Scopus, *dan* ScienceDirect, *dengan proses skrining berdasarkan kriteria inklusi dan eksklusi. Literatur yang terpilih dikaji secara kritis menggunakan kriteria* Oxford Centre for Evidence-based Medicine *untuk studi etiologi.* ***Hasil:*** *Ditemukan dua studi potong lintang yang sesuai dengan PICO dan kriteria inklusi dari laporan kasus ini. Kedua studi tersebut menunjukkan pola disfungsi sistem saraf otonom, yang ditandai dengan peningkatan aktivitas parasimpatis dan penurunan aktivitas simpatis, pada pasien rinitis alergi.* ***Kesimpulan:*** *Hasil penelitian ini menunjukkan bahwa disfungsi sistem saraf otonom berperan dalam patofisiologi rinitis alergi, sebagaimana dibuktikan oleh perubahan dalam variabilitas denyut jantung (*HRV*).*

Kata kunci: *disfungsi otonom, rinitis alergi, heart rate variability*

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INTRODUCTION

Allergic rhinitis is an inflammatory disease of the nasal mucosa caused by an allergic reaction to inhalant allergens, mediated by IgE.[1] The prevalence of allergic rhinitis reaches up to 40% in the global population, and is characterized by symptoms such as nasal congestion, rhinorrhea, nasal itching, and sneezing. This condition impacts the quality of life, including sleep disturbances, and affects school or work performance.[2-4]

Autonomic nervous system dysfunction plays a significant role in the pathophysiology of allergic rhinitis. Allergic rhinitis can cause an imbalance in the autonomic nervous system, marked by increased parasympathetic activity and decreased sympathetic activity. Excessive activation of the parasympathetic system is characterized by increased vagal release of nitric oxide, which triggers inflammation through Th2 (T helper 2) cells proliferation. Increased vagal activity also leads to vasodilation and mucus hypersecretion in the nasal passages, resulting in symptoms such as nasal congestion and rhinorrhea.[5-7]

Autonomic nervous system function can be assessed through heart rate variability (HRV), a non-invasive method that reflects the autonomic system's response to environmental changes and physiological conditions.[6] Several studies have evaluated HRV in patients with allergic rhinitis. A study by Kim et al.[6] indicated that patients with mild intermittent allergic rhinitis exhibited increased parasympathetic and decreased sympathetic activity, with this dominance reduced in patients with moderate to severe persistent allergic rhinitis. Another study by Lan et al.[7] demonstrated poor sympathetic modulation in sitting positions in allergic rhinitis patients compared to controls, suggesting autonomic dysfunction's role in allergic rhinitis pathophysiology. Buekers et al.[4] found that increased daily allergy symptom scores were associated with elevated resting heart rates the following day. This study aimed to evaluate autonomic nervous system dysfunction in allergic rhinitis patients using HRV.

CASE REPORT

A 28-year-old female patient complained of runny nose with clear, watery mucus for the past year. The symptom was accompanied by alternating nasal congestion, especially on the left side, which worsens during cold weather or exercise. She often sneezed in the morning, experienced intermittent nasal itching, snored while sleeping, and frequently woke up due to nasal congestion. There was no history of breathing difficulties during sleep. These complaints disrupted her daily activities and sleep. The patient had a total nasal symptom score (TNSS) of 9, a nasal obstruction symptom evaluation (NOSE) score of 30, an Epworth Sleepiness Scale (ESS) score of 11, and a reflux symptom index (RSI) score of 19.

Physical examination revealed a body mass index of 33.8 (grade 2 obesity), with vital signs within normal limits. Both nasal cavities were narrow, with oedematous inferior turbinates, smooth and livid mucosa, open middle meatus, and no secretion in the middle meatus. Throat examination showed symmetrical pharyngeal arches, midline uvula, bilateral grade 3 tonsils, and a tranquil posterior pharyngeal wall. Rhinopharyngolaryngoscopy revealed narrow nasal cavities, oedematous and livid inferior turbinates, serous secretions visible, no secretion in the osteomeatal complex, tranquil

nasopharynx, 30% adenoid hypertrophy, and grade 1 lingual tonsil hypertrophy. Her epiglottis was upright, no penetration or aspiration observed. Both glottic and vocal cord movements were symmetrical during static and dynamic states. A skin prick test yielded positive results for *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Aspergillus*. Heart rate variability assessment indicated increased parasympathetic activity, and decreased sympathetic activity.

The patient was diagnosed with moderate to severe persistent allergic rhinitis, tonsil hypertrophy, laryngopharyngeal reflux, and high-risk obstructive sleep apnea. Treatment included nasal irrigation with sodium chloride 0.9%, fluticasone furoate nasal spray, and cetirizine.

CLINICAL QUESTION

The clinical question based on the case report above: Is autonomic nervous system dysfunction associated with allergic rhinitis?

P: Patients with allergic rhinitis

I: Autonomic nervous system dysfunction (as assessed by HRV)

C: Individuals without allergic rhinitis

O: Increased severity of allergic rhinitis symptoms

Type of question: Etiologic

Type of study: Systematic review/meta-analysis for etiologic study, cohort, case-control, and cross-sectional study

METHOD

A literature search was conducted on March 23, 2024, using four databases: PubMed, EBSCO, Scopus, and ScienceDirect. The keywords used included "allergic rhinitis," "autonomic nervous system dysfunction," and "heart rate variability," along with synonyms of these terms (Table 1). The inclusion criteria comprised studies involving patients diagnosed with allergic rhinitis that assessed autonomic nervous system function through heart rate variability, and study types including systematic reviews/meta-analyses, cohort studies, and case-control studies. Exclusion criteria encompassed studies irrelevant to the clinical question, and articles in languages other than English.

Critical appraisal was conducted on selected articles based on the 2011 Oxford Centre for Evidence-based Medicine criteria for etiologic studies. The standard validity criteria for research assess aspects of validity, importance, and applicability (VIA) (Table 2). Each article was independently appraised by two reviewers to minimize subjective bias, to ensure consistency between reviewers, and to improve the reliability and transparency of the critical appraisal process.

Table 1. Literature search strategy

Database	Search strategy	Hits (articles)
PubMed	((Rhinitis, Allergic[MeSH Terms]) OR (Allergic Rhinitis*[Text Word])) AND (Autonomic Nervous System Diseases[MeSH Terms]) OR (Autonomic Nervous System Diseases[Text Word])) OR (Sympathetic Nervous System Diseases[Text Word])) OR (Parasympathetic Nervous System Diseases[Text Word])) OR (Segmental Autonomic Dysfunction[Text Word])) OR (ANS disease*[Text Word]))	11
EBSCO	AB (allergic rhinitis or hay fever or nasal allergy) AND AB (autonomic nervous system dysfunction OR autonomic nervous system diseases OR sympathetic nervous system diseases OR parasympathetic nervous system diseases OR ANS diseases) AND AB (heart rate variability or HRV or heart rate variation)	7

ProQuest	abstract(allergic rhinitis or hay fever or nasal allergy) AND abstract(autonomic nervous system dysfunction OR autonomic nervous system diseases OR sympathetic nervous system diseases OR parasympathetic nervous system diseases OR ANS diseases) AND abstract(heart rate variability or HRV or Heart rate variation)	3
Science Direct	(allergic rhinitis or hay fever or nasal allergy) AND (autonomic nervous system dysfunction OR autonomic nervous system diseases OR sympathetic nervous system diseases OR parasympathetic nervous system diseases OR ANS diseases) AND (heart rate variability or HRV or Heart rate variation)	7

Table 2. Included studies characteristics

Author, year	Country	Study design	N	Population	Intervention	Comparation	Outcome
Lan et al., 2013	Taiwan	Cross-sectional	11 allergic rhinitis patients, 13 controls	Patients aged 19-39 years old with diagnosis of allergic rhinitis from positive specific IgE results	Allergic rhinitis	Without allergic rhinitis	Heart Rate Variability (frequency domain analysis)
Kim et al., 2016	Korea	Cross-sectional	32 allergic rhinitis patients, 32 controls	Patients aged >18 years old with symptoms of allergic rhinitis and positive skin prick test	Allergic rhinitis	Without allergic rhinitis	Heart Rate Variability (frequency domain analysis)

RESULT

The literature search across four databases identified 11 articles from PubMed, 7 from EBSCO, 3 from ProQuest, and 7 from ScienceDirect. A total of 28 articles were filtered for duplicates, identifying 11 overlapping articles. Subsequently, the titles and abstracts of the remaining 17 articles were screened, yielding 4 articles. Full-text screen was performed, resulting in 2 articles eligible for critical review. The flow of the literature search and article selection is illustrated in Figure 1.

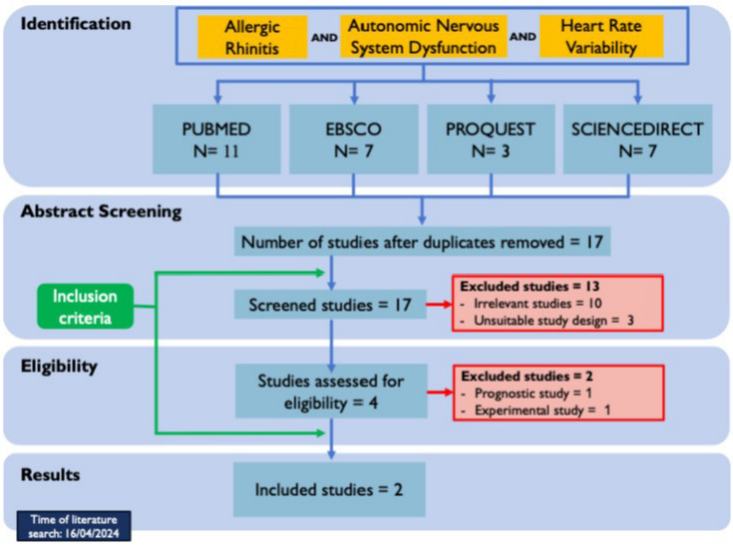

Figure 1. Literature search flow diagram

Based on the literatures search, two studies were found to be relevant to the PICO and eligibility criteria. The characteristics of these studies were summarized in Table 2. The study by Lan et al.[7] assessed autonomic nervous system activity in allergic rhinitis patients using heart rate variability (HRV) analysis. The inclusion criteria for this study were adults aged 19-39 years with a diagnosis of allergic rhinitis based on clinical symptoms and positive specific IgE results. Exclusion criteria included patients with nasal polyps, sinusitis, or comorbidities such as asthma, diabetes mellitus, hypertension, stroke, and autoimmune diseases. The study subjects consisted of 24 participants, comprising 11 allergic rhinitis patients and 13 healthy controls. The second study by Kim T et al.[6] compared the autonomic nervous system in patients with allergic rhinitis and healthy individuals. Inclusion criteria were patients aged 18 years or older, with symptoms of allergic rhinitis such as rhinorrhea, nasal obstruction, nasal pruritus, and recurrent sneezing, as well as positive skin prick test results. Exclusion criteria were patients with rhinosinusitis, nasal polyps, recent use of asthma medications, antihistamines, corticosteroids, decongestants, or leukotriene receptor antagonists, and those with conditions affecting HRV, such as cardiovascular, endocrine, neurological, or psychiatric disorders. A total of 32 participants were enrolled in this study.

Critical appraisal of the two included studies was performed in terms of validity, importance, and applicability. The validity appraisal of the two included studies demonstrated several strengths and limitations. Both studies by Lan et al.[7] (2013) and Kim et al.[6] (2016) clearly defined their study groups through well-specified inclusion and exclusion criteria, with control groups matched for age and sex. In both studies, the exposure and outcomes were measured consistently across groups using standardized heart rate variability (HRV) assessments with ECG recordings in the sitting position for five minutes, which supported internal validity. However, since both were cross-sectional studies, they lacked follow-up, making it impossible to establish temporality or determine whether autonomic dysfunction preceded allergic rhinitis. Neither study applied a dechallenge–rechallenge approach, and only Kim et al.[6] provided evidence of a dose-response gradient by comparing HRV parameters across subgroups with different disease severities. Despite these limitations, the findings were biologically plausible and consistent with prior literatures, supporting an association between autonomic nervous system dysfunction and allergic rhinitis.

The importance appraisal of both studies demonstrated consistent alterations in autonomic function among patients with allergic rhinitis. Lan et al.[7] reported that, in the sitting position, patients with allergic rhinitis exhibited significantly higher RR intervals, lower LF power, and a reduced LF/HF ratio compared with healthy controls, indicating a shift toward parasympathetic dominance. Similarly, Kim et al.[6] found that patients with intermittent allergic rhinitis had significantly higher HF and NHF values, alongside a markedly lower LF/HF ratio compared with controls, reflecting enhanced parasympathetic activity. Moreover, NHF was significantly lower in intermittent allergic rhinitis compared with persistent allergic rhinitis, suggesting potential differences in autonomic regulation across disease subtypes. Altogether, these findings highlighted the clinical relevance of autonomic dysfunction in allergic rhinitis, and supported the importance of HRV analysis in this population. The study results were applicable, as the populations involved adults with allergic rhinitis undergoing HRV assessment, consistent with the clinical setting. The critical appraisal of each study was presented in Table 3.

Table 3. Critical appraisal

			Validity								Importance	Applicability
Article	**Study Design**	**N**	*Similarity between two groups*	*Measured in the same way*	*Adequate and complete follow-up*	*Exposure preceded the outcome*	*Dosage response gradient*	*Re-challenge de-challenge*	*Consistency*	*Biological Sense*	*Comparison*	*Similarity*
Lan et al., 2013	Cross-sectional	11 RA patients, 13 controls	+	+	-	-	-	-	+	+	• RR interval in RA > controls (p<.001) • LF in RA < controls (p=.023) • LF/HF in RA < controls (p= .044)	+
Kim et al,[6] 2016	Cross-sectional	32 RA patients, 32 controls	+	+	-	-	+	-	+	+	• HF and NHF in RA > controls (p<.05) • NLF and LF/HF in RA < controls (p<.05)	+

DISCUSSION

This report identified two studies that was directly relevant to the clinical question regarding the association between autonomic nervous system dysfunction and allergic rhinitis. The study by Lan et al.[7] demonstrated that patients with allergic rhinitis exhibited impaired sympathetic modulation, as reflected by a significant reduction in LF and LF/HF ratio in the sitting position compared with healthy controls, despite no significant differences in HRV parameters in the supine position. These findings suggested that autonomic dysfunction in allergic rhinitis may be posture-dependent, with reduced sympathetic activity becoming more evident during physiological stress. Similarly, the study by Kim et al.[6] reported that parasympathetic activity predominated in patients with mild and intermittent allergic rhinitis, whereas prolonged disease duration and increased severity were associated with a shift toward sympathetic predominance. This indicated a dynamic imbalance of autonomic regulation in allergic rhinitis, in which parasympathetic hyperactivity might characterize the early phase of the disease, while sympathetic activation emerged with chronicity and greater symptom burden.

Allergic rhinitis is a chronic inflammatory condition of the nasal mucosa triggered by a type I hypersensitivity reaction after exposure to specific inhalant allergens.[3] Neurogenic inflammation is one mechanism

involved in its pathophysiology, where the interaction between the nervous and immune systems leads to increased nerve sensitivity and inflammation.[1,8] Autonomic nervous system dysfunction in allergic rhinitis involves imbalances in sympathetic and parasympathetic activity, affecting nasal and systemic responses. Parasympathetic activity increases mucus secretion and vasodilation, while sympathetic activity reduces secretion and causes vasoconstriction.[1,8]

Heart rate variability (HRV) assessment, marked by reduced SDNN and an imbalanced LF/HF ratio, was used to evaluate autonomic dysfunction. Studies showed parasympathetic dominance in allergic rhinitis. Won et al.[9] found a significantly lower LF/HF ratio in allergic rhinitis patients, indicating reduced sympathetic activity. Similarly, Kim et al.[6] and Lan et al.[7] reported lower LF/HF ratios, showing poor sympathetic modulation in allergic rhinitis patients, especially in sitting positions.

Autonomic imbalance in allergic rhinitis leads to excessive parasympathetic stimulation, vagal activity, and weakened sympathetic activity. Parasympathetic overstimulation increases nasal mucus secretion and vasodilation, causing nasal congestion and rhinorrhea. Conversely, reduced sympathetic activity contributes to nasal tissue swelling and edema, worsening congestion.[6] Excessive vagal activity also releases nitric oxide, promoting Th2 lymphocyte proliferation and pro-inflammatory activity, aggravating allergic conditions.

HRV and inflammatory marker studies showed a complex interaction between the autonomic nervous and immune systems. A negative correlation exists between HRV parameters and inflammatory markers. For example, reduced HF (parasympathetic activity) is linked to increased inflammatory markers like CRP.[6,10] Parasympathetic activity inhibits inflammation through cholinergic anti-inflammatory pathways, while sympathetic activity is pro-inflammatory.

In this study, heart rate variability analysis revealed increased parasympathetic activity and decreased sympathetic activity. This was evident from the low LF/HF ratio, indicating parasympathetic dominance. The strength of both studies lay in the use of HRV as an objective and non-invasive marker of autonomic function, supported by strict inclusion and exclusion criteria. However, small sample sizes, cross-sectional designs, and limited generalizability remained important limitations. Further studies with larger sample sizes and diverse populations are needed to confirm these findings, and to explore the potential of heart rate variability as a clinical biomarker for disease monitoring and treatment response.

In conclusion, based on the critical review of the two journals, it could be concluded that autonomic nervous system dysfunction might have a possible relationship with allergic rhinitis. Patients with allergic rhinitis might exhibit autonomic imbalance, characterized by increased parasympathetic activity and decreased sympathetic activity.

CONFLICT OF INTEREST

The authors declared no conflict of interest to disclose.

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