Original Article

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# Autonomic Functions in Patients with Allergic Rhinitis: A Cross-sectional Observational Study

Physiology Section

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## ABSTRACT

**Introduction:** Allergic Rhinitis (AR) is an inflammatory disease of the nasal membranes characterised by nasal congestion, itching, rhinorrhoea, and sneezing. One of the primary factors contributing to the development of AR symptomatology is neurological. Both the Central Nervous System (CNS) and the Autonomic Nervous System (ANS) play important roles in the symptomology of such hypersensitivity reactions.

**Aim:** To assess and compare the cardiac autonomic functions in AR patients with healthy controls.

**Materials and Methods:** The present cross-sectional observational study was conducted in the Department of Physiology, SMS Medical College, Jaipur, Rajasthan, India from December 2021 to June 2022. Forty AR patients from the Ear, Nose and Throat (ENT) Department and 40 age and gender-matched healthy controls were enrolled from the employees working at SMS Medical College, Jaipur, Rajasthan, India. Parasympathetic function tests like the expiration to inspiration ratio, Valsalva ratio, and sympathetic function tests like Blood Pressure (BP) response to standing and BP response to sustained hand grip were performed and compared to assess the functional status of ANS in cases and controls. Primer version 6.0 was used for statistical analysis. The unpaired t-test was applied to the data of both groups, and a p-value <0.05 was considered statistically significant.

**Results:** The increase in Diastolic BP (DBP) during isometric hand grip exercise was significantly lower in AR patients (p-value <0.001). The decrease in Systolic BP (SBP) upon immediate standing was higher in the AR group (p-value <0.001). The expiration to inspiration ratio and valsalva ratio were also significantly higher (p-value <0.05) in AR patients compared to the healthy controls.

**Conclusion:** Patients with AR have relatively reduced sympathetic reactivity and escalated parasympathetic reactivity towards autonomic function tests compared to apparently healthy individuals. The ANS, affected in patients with AR, puts them at a greater risk of subsequent cardiovascular morbidity. Therefore, early assessment of autonomic functions should be considered for the early detection and management of such morbidities.

**Keywords:** Cardiovascular morbidity, Isometric exercise, Parasympathetic nervous system

## INTRODUCTION

AR is a prevalent yet underappreciated inflammatory disorder of the nasal mucosa, characterised by pruritus, sneezing, rhinorrhoea, and nasal congestion [1]. The disease burden of AR is enormous, constituting about 55% of all allergies reported worldwide [2]. In the context of India, almost 20-30% of the population suffers from atleast one allergic disease, and the reported incidence of AR in India ranges between 20-30% [3]. AR is an inflammatory disorder of the upper airways; however, inflammation alone is not sufficient to explain the chronic nature of the disease. Being a multifactorial disorder, AR manifests through a complex interplay of various interrelated causative factors, among which one of the most important is the involvement of the neurological system, primarily the autonomic part. Although it has already been proven that such derangements in the neurological system play a pivotal role in the symptomology of hypersensitivity reactions, the exact mechanism remains to be elucidated [4]. Many other disorders are also associated with AR, such as asthma, atopic dermatitis, sinusitis, otitis media, and nasal polyposis [5]. The cost of treating these conditions must be considered when evaluating the socio-economic impact of AR [6]. The effects of AR are not just limited to hampered quality of life; they also affect school performance, work performance, socialisation, as well as sleep [7,8].

The ANS regulates many important functions in humans, such as BP, heart rate, thermoregulation, respiration, gastrointestinal function, bladder function, sexual function, and the reactivity of the nasal and sinus mucous membranes, as well as the glands. The adrenergic fibers of the Sympathetic Nervous System (SNS) control vasoconstriction of the nasal mucosa, and the cholinergic fibers of the Parasympathetic Nervous System (PNS) are responsible for vasodilation and mucosal gland functioning [9]. Therefore, AR may represent either hyperfunction of the PNS in the nose and paranasal sinuses or an imbalance between the PNS and SNS [10]. Along these lines, prior studies have reported a higher rate of parasympathetic predominance in patients with AR compared to healthy controls [11,12]. Some studies have investigated the association between ANS functioning and AR severity in children and adults, wherein the researchers have observed increased vagal hyperactivity with increased AR severity [13,14].

Evaluation of cardiac autonomic functions can be conducted through various tests, including Ewing's Battery of tests [15]. These tests encompass heart rate responses to the Valsalva maneuver, heart rate responses to standing, heart rate responses to deep breathing, BP response to standing, and BP response to sustained hand grip. The present study aimed to utilise this range of tests to elucidate the involvement of the ANS in patients with AR. This would provide a logical and plausible justification for explaining the cause-and-effect relationship and progression of AR symptomatology. Additionally, it could assist in assessing cardiovascular risk, as well as detecting and preventing complications associated with cardiac autonomic dysfunctions such as arrhythmia and myocardial infarction in these patients. Therefore, the present study aimed to assess the cardiac autonomic functions in AR patients and compare them with those of healthy controls.

## MATERIALS AND METHODS

The present study was a hospital-based cross-sectional observational study conducted at the Department of Physiology, SMS Medical College, Jaipur, Rajasthan, India from December 2021 to June 2022. Prior approval was obtained from the Institutional Ethics Committee

(IEC) (1104/MC/EC/2021, dated 1/12/2021) and the institutional research review board. A written informed consent was obtained from all the subjects before commencing any test procedures.

**Inclusion criteria:** Diagnosed cases of AR and healthy subjects aged between 25-35 years, who were co-operative and willing to participate in the study were included in the study.

**Exclusion criteria:** Subjects with any acute or chronic illnesses (such as Diabetes Mellitus, Hypertension, etc.) known to affect ANS function, a history of prior drug intake (such as anticholinergic, etc.) known to affect ANS function, smokers, and alcoholics were excluded from the study.

**Sample size:** A sample size of 12 subjects in each group was initially calculated at a 95% confidence interval and 80% power to detect an expected difference of 1.0 ms2 and 0.81 ms2 in mean HF power and SD values, respectively, in frequency domain analysis between the intermittent AR group and the healthy control group, as reported in the reference article [14]. However, for the present study, a sample size of 40 subjects in each group (AR group and control group) was chosen.

Hence, a total of 80 subjects were enrolled in the study and divided into two groups. Group one (AR group) included 40 diagnosed cases of AR patients from the Department of Otorhinolaryngology, SMS Medical College and Hospital, Jaipur. Group two (control group) included 40 age- and gender-matched healthy controls who were employees working at SMS Medical College, Jaipur.

### Procedure

Anthropometric parameters such as height, weight, and Body Mass Index (BMI) were measured. BMI was calculated using the formula: Weight (Kg)/Height ($m^2$) [16]. Autonomic function assessment (parasympathetic and sympathetic reactivity tests) was performed, along with the prior assessment of resting SBP and DBP in all subjects. Parasympathetic reactivity tests included heart rate response to deep breathing (expiration/inspiration ratio) (normal range >1.21) and valsalva ratio (normal range >1.21) [15]. Sympathetic reactivity tests included orthostatic fall in SBP (mmHg) (normal <10 mmHg) and increase in DBP after sustained handgrip (mmHg) (normal >16 mmHg) [15].

**ANS function assessment:** The subjects were instructed to abstain from consuming caffeine and/or meals for atleast two hours prior to the test procedure. The subjects were made to lie down comfortably in the ANS function laboratory, in a quiet environment with an ambient room temperature of 25°C. Cardiovascular autonomic function assessment was performed according to Ewing's battery [15] of tests using the RMS CANWIN (cardiac autonomic neuropathy analyser) machine in the morning hours, ensuring a minimum resting phase of 15 minutes for each subject. Detailed clinical history was recorded, and an examination was conducted.

## STATISTICAL ANALYSIS

The statistical analysis was performed using 'Primer software' version 6. Quantitative data were expressed as mean±SD. An unpaired t-test was used to compare the autonomic function tests, including E:I ratio, valsalva ratio, resting SBP and DBP, orthostatic fall in SBP, and increase in DBP after sustained hand grip. Statistical significance was considered at a p-value <0.05, and highly significant at a p-value <0.001.

## RESULTS

The mean age of subjects in the case group was 30.33±3.28 years, while for the controls, it was 29.65±3.50 years. Both groups had 22 males and 18 females. The subjects were also comparable in terms of height, weight, and BMI, and no statistically significant difference was observed between the two groups [Table/Fig-1].

The change in DBP during sustained handgrip exercise [Table/Fig-2] was significantly lower in AR patients (6.08±4.51 mmHg) compared to the controls (17.73±5.75 mmHg). The fall in SBP upon immediate standing was higher in the AR group (9.75±3.81 mmHg) compared to the controls (0.45±4.10 mmHg), and the difference was statistically highly significant (p-value <0.001). The E:I ratio and Valsalva ratio showed a significant (p-value <0.05) increase in AR patients compared to the healthy controls.

| Parameter | Groups (means±SD) | | p-value |
|---|---|---|---|
| | Case group (N-40) | Control group (N-40) | |
| Age (years) | 30.33±3.28 | 29.65±3.50 | 0.37 |
| Males | 22 | 22 | |
| Females | 18 | 18 | |
| Height (m) | 1.62±0.10 | 1.64±0.11 | 0.39 |
| Weight (Kg) | 56.33±9.87 | 61.05±14.84 | 0.098 |
| BMI ($Kg/m^2$) | 21.51±3.13 | 22.63±4.21 | 0.192 |

**[Table/Fig-1]:** Anthropometric parameters of both groups.
Test applied: Unpaired t-test; *Statistically significant p-value <0.05

| Parameter | Groups (means±SD) | | p-value |
|---|---|---|---|
| | Case group (N-40) | Control group (N-40) | |
| E:I Ratio | 1.40±0.24 | 1.25±0.14 | 0.015* |
| Valsalva ratio | 1.52±0.38 | 1.34±0.20 | 0.012* |
| Resting systolic BP (mmHg) | 114.25±8.9 | 113.28±7.95 | 0.61 |
| Resting diastolic BP (mmHg) | 74.50±10.8 | 70.15±9.50 | 0.061 |
| Orthostatic fall in systolic BP (mmHg) | 9.75±3.81 | 0.45±4.10 | 0.0004** |
| Increase in diastolic BP after sustained handgrip (mmHg) | 6.08±4.51 | 17.73±5.75 | 0.0005** |

**[Table/Fig-2]:** Autonomic function tests parameters of both groups. Comparison of autonomic function tests parameters in case (allergic rhinitis) and Control group.
Test applied: Unpaired t-test; *statistically significant p-value <0.05; **Statistically highly significant p-value <0.001

## DISCUSSION

The present study aimed to investigate the association between ANS dysfunction and symptomatology of AR. The AR group exhibited increased parasympathetic reactivity, as evidenced by higher E:I ratio (1.40±0.24) and Valsalva ratio (1.52±0.38), compared to the healthy controls, where the values for these parameters were 1.25±0.14 and 1.34±0.20, respectively. Additionally, there was a blunting of sympathetic reactivity, indicated by a reduced rise in DBP response during the SHG test (6.08±4.51 mmHg in AR group vs. 17.73±5.75 mmHg in controls) and an increased fall in SBP upon active standing (9.75±3.81 mmHg in AR group vs. 0.45±4.10 mmHg in controls). The difference in E:I ratio between the case and control groups was statistically significant, suggesting increased parasympathetic reactivity in AR patients.

A study conducted by Ishman SL et al., also reported similar findings of sympathetic hypofunction and absent parasympathetic dysfunction, but in terms of heart rate response to deep breathing [11]. In contrast, the present study showed similar results of sympathetic hypofunction but higher parasympathetic reactivity in AR patients compared to controls. This discrepancy may be attributed to differences in subject selection and duration of illness among AR patients.

The present study demonstrated a statistically significant difference in the Valsalva ratio between the case group and control group (1.52±0.38 in AR patients compared to 1.34±0.20 in controls, with a p-value of 0.012). However, studies conducted by Ishman SL et al., and Emin O et al., contradicted these results, as they found no statistically significant difference in the Valsalva ratios [11,13]. The discrepancy in findings may be attributed to differences in subject selection and the range of illness duration in these studies.

The findings of the present study suggest sympathetic hypofunction and parasympathetic predominance in patients with AR, indicating

a potential similar association in other allergic disorders. Boettger MK et al., and Cicek D et al., found sympathetic hypofunction and parasympathetic predominance in patients with atopic dermatitis, suggesting increased parasympathetic and decreased sympathetic activity in allergic diseases [17,18]. Similarly, Lutfi MF and Gupta J et al., concluded in their study that asymptomatic asthmatic subjects (another disease within the realm of allergic disorders) exhibited significantly elevated central parasympathetic outflow and concurrently reduced central sympathetic outflow compared to the control group [19,20].

The present study's findings of sympathetic hypofunction and parasympathetic predominance in AR patients were consistent with a study conducted by Emin O et al., who demonstrated a positive correlation between disease severity in children with AR and ANS dysfunctions and observed significantly abnormal autonomic dysfunction patterns in children with AR, indicating increased parasympathetic activity [13]. Moreover, the results of the present study also suggest a similar autonomic dysfunction pattern in AR patients, albeit in adults. These findings align with a study by Kim MH et al., where the authors indicated predominant parasympathetic nervous activity in patients with mild and intermittent AR [14].

The present study proposes a definite involvement of the ANS in AR patients by demonstrating a statistically significant difference in ANS test parameters using a standardised Ewing's battery of tests. The cardiovascular autonomic reactivity methods employed in this study suggest compromised status in both the sympathetic and parasympathetic divisions of the ANS. Therefore, it is recommended to assess ANS functions early to prevent potential adverse outcomes of autonomic dysfunction, such as peripheral vascular disease, myocardial infarction, and ischaemic heart disease, in patients with AR.

### Limitation(s)

The present study did not classify the disease based on disease duration and severity, and therefore, no intergroup comparisons were made. As a result, the obtained results are only sufficient for making a broad comparison of ANS dysfunction between the AR group and apparently healthy normal controls.

## CONCLUSION(S)

The present study observed an enhanced reactivity of the parasympathetic division and a blunted reactivity of the Sympathetic Nervous System (SNS) in patients with AR. These findings also help explain the observation that both resting SBP and DBP were more disturbed in AR patients, along with higher blood pressure changes. The impaired functioning of the ANS in AR patients increases their cardiovascular risk, highlighting the need for early assessment of ANS functions. This early assessment could potentially prevent overall morbidity in AR patients and play a crucial role in the early detection and timely management of severe consequences of cardiac autonomic dysfunction, such as ischaemic heart disease, peripheral vascular disease, and myocardial infarction.

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