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Original Research Article

Analysis of Heart Rate Variability Using Frequency Domain Parameters in Patients with Allergic Rhinitis

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Abstract

Introduction: Allergic rhinitis (AR) is an inflammatory disease of nasal membranes characterized by symptoms like nasal congestion, itching, rhinorrhea, and sneezing. AR constituting almost 55% of all allergies. AR incidence in India lies somewhere between 20% to 30%. One of the primary factors towards development of AR symptomatology happens to be neurological. The objective of the present study was to assess such associations of cardiac autonomic functions in AR patients and their subsequent comparison with healthy controls subjects via frequency domain parameters of heart rate variability analysis.

Methodology: The present study was conducted in the Department of Physiology, SMS Medical College, Jaipur wherein forty AR patients (both males and females) were recruited from the ENT Department and forty age- and gender-matched healthy subjects were taken for comparison. HF (ms^2) and HF (n.u.) used for Parasympathetic function; LF (ms^2) and LF (n.u.) used for sympathetic function and LF/HF ratio used for sympathovagal balance.

Results: Values of LF (ms^2) and LF (n.u.) significantly lower in AR patients ($P < 0.05$) whereas, values of HF (ms^2) and HF (n.u.) was Significantly higher in AR group ($P < 0.05$). The LF/HF ratio was significantly lower ($P < 0.05$) in AR patients as compared to the healthy controls.

Statistical Analysis: Unpaired 't' test was applied for statistical analysis of data of both groups where P valve <0.05 considered as statistically significant.

Conclusions: Our study indicated that patients with allergic rhinitis have escalated Parasympathetic reactivity and blunted sympathetic reactivity along with diminished Sympathovagal balance which represent as hypervagal activity as compared to the apparently healthy normal individual.

Keywords: Rhinitis Allergic, Heart Rate Variability, Frequency domain Parameter, Sympathetic Nervous system, Parasympathetic Nervous system.

Introduction

Allergic rhinitis is a prevalent yet underappreciated inflammatory disorder of nasal mucosa, which is characterized by pruritus, sneezing, rhinorrhea, and nasal congestion.[1] The burden of Allergic Rhinitis is enormous, constituting about 55%

of all allergies reported worldwide. Whereas, in India almost 20-30% of Indian population suffers from at least one allergic disease. Talking specifically of AR in India, the reported incidence of allergic rhinitis also ranges between 20% and 30%.[2]

Many other disorders are also associated with Allergic Rhinitis. These are mainly Asthma, Atopic Dermatitis, Sinusitis, Otitis Media, Nasal Polyposis, and Dental Occlusion. The cost of treating these conditions must be taken into account while evaluating the socio-economic impact of allergic rhinitis.[3] The effect of AR is not just limited towards hampered quality of life but it also affects school performance, work performance, socialization as well as sleep.

In Allergic Rhinitis, various inflammatory cells, including mast cells, B cells, macrophages, and eosinophils infiltrate the nasal lining upon exposure to an inciting allergen (most commonly airborne dust, mite, animal dander, cockroach residues and pollens).[4]

Allergic Rhinitis was previously classified on the basis of Time of exposure, into seasonal, perennial, and occupational, however this classification did not stand well in the test of time with an ever-increasing scientific acumen and understanding hence is superseded by a recent classification of allergic rhinitis, suggested by ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines [5] is on the basis of:

1. Duration, Classifying as “Intermittent” or “Persistent” disease,

2. Severity of symptoms and the quality of life, Classifying as “Mild” or “Moderate-Severe” disease.

In terms of definition, Allergic Rhinitis is defined as an inflammatory disorder of the upper air-ways, however inflammation alone is not sufficient to explain the chronic nature of the disease. Allergic Rhinitis being a multifactorial disorder, embarks its manifestation on a complex interplay of various interrelated causative factors among which one of the most important one is the involvement of neurological system primarily the autonomic part. Although it has been already been proven that such derangements in the neurological system play a pivotal role in the symptomology of hypersensitivity reactions, but the exact mechanism remains to be elucidated.[6]

Autonomic Nervous System regulates the reactivity of the nasal and sinus mucous membranes and the glands as well. 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 vasodilatation and mucosal gland function [7]. Thus, Allergic Rhinitis represents as either hyperfunction of the PNS in the nose and paranasal sinuses or an imbalance between PNS and SNS [8].

It has been proposed that dysfunction of autonomic nervous system (ANS) is an important factor underlying Allergic Rhinitis. Some studies reported a higher reactivity of parasympathetic predominance in patients with Allergic Rhinitis than in healthy controls [9,10]. Another study investigated the association between ANS function and AR severity in children; the researchers assessed ANS activity using the sympathetic skin response and R-R interval variation and the results indicate that vagal hyperactivity increased with AR severity [11].

Amidst the various noninvasive techniques for evaluating the autonomic status, HRV has emerged as a simple, noninvasive method to evaluate the sympathovagal balance at the Sino-atrial level and most widely performed for measuring of autonomic function.[12] This test generates a definite, sensitive and reproducible indirect measure of autonomic reactivity on cardiac functions. Under

frequency domain analysis (HRV frequency spectra), the HF component is attributed to parasympathetic influences on the heart and LF component is due to both parasympathetic nervous system (PNS) and sympathetic nervous system (SNS) activity.[13]

Impact of the Allergic rhinitis on cardiovascular function can be assessed using the HRV analysis. A better way for understanding the autonomic status short term HRV analysis is from a 5 min record of ECG. Allergic rhinitis has been proved to alter the ANS by many studies published. [10,11]

Despite many attempts made in order to elucidate the exact pathophysiology of AR, the exact cause and effect relationship justifying the logical progression of the AR symptomatology due in to a causative sequel is still obscure and elusive, hence the present study is aimed towards deciphering a possible association of dysregulated autonomic functioning as a cause of AR symptomatology complex using a standardized mode of HRV analysis. This might also help in assessment of cardiovascular risk and early detection & prevention of complications possible due to cardiac autonomic dysfunctions such as Arrythmia and Myocardial In-fraction etc.)

Material and Methods

The present study was a hospital-based cross-sectional type of comparative, observational study conducted on forty Allergic Rhinitis patients in the age group of 25–35 years and forty age- and gender-matched healthy controls. Diagnosed Allergic Rhinitis patients were recruited from the Department of Otorhinolaryngology, SMS Medical College and attached group of Hospitals, Jaipur. Age- and gender-matched healthy controls were chosen from the employees working at SMS Medical College, Jaipur. Prior approval was obtained by the institutional ethics committee and institutional research review board. A written informed consent was obtained from all the subjects before commencing with any procedure.

Inclusion criteria for (Case/Control) Group:

1. Diagnosed case of AR (for being included in Case group)
2. Apparently healthy subjects (for being included in Control group)
3. Aged 25-35 years.
4. Subjects who are cooperative and giving informed written consent.

Exclusion Criteria for both groups :

1. Acute or chronic illness (like Diabetes Mellitus, Hypertension etc.) known to affect ANS functions.
2. Person taking drugs (like Anticholinergic etc.) known to affect ANS functions.
3. Smokers
4. Alcoholics

Heart rate Variability (HRV)

The assessment of the heart rate variability was done by recording with polygraph (RMS Polyrite D, version 1.0) based on the principle of EKG.

For short term analysis of HRV, ECG was recorded in the supine posture for 5 minutes after 15 minutes of supine rest in a quiet environment.

The analogue ECG signals were converted to digital signal and stored in the computer offline for frequency and time domain analysis. In the frequency domain analysis, the power spectrum for HRV was calculated using the Fast Fourier Transformation (FFT) based method.[13]

Following parameters were included in the study:

Frequency domain HRV parameter

- LF n.u. (normalized unit) in %
- LF (ms^2)
- HF n.u. (normalized unit) in %
- HF (ms^2)

- LF/HF ratio

Statistical Analysis

Quantitative data were expressed as mean ± SD. The data so obtained was statistically analyzed using the 'Primer software' version 6. The Unpaired 't'-test was applied for statistical analysis of the results. Statistical significance was assigned at a p value < 0.05 and highly significant at a p valve < 0.001.

Results

[Table 1] Shows the baseline characteristics of Allergic Rhinitis (Case) group and control groups. Anthropometric parameters (like Age, height, weight, and body mass index) did not show any statistically significant difference between the two groups. Values of LF (n.u.) and LF (ms^2) [Table 2, Fig. 1] (measure of sympathetic reactivity), was significantly lower in Allergic Rhinitis patients as compared to the controls. HF (n.u.) and HF (ms^2) (indicator of parasympathetic reactivity) was higher in Allergic Rhinitis group as compared to controls, and the difference was statistically significant (P < 0.05). LF/HF (measure of sympathovagal response) decreased in Allergic Rhinitis patients as compared to the healthy controls which shows autonomic imbalance in AR patients.

Table 1: Anthropometric Parameters of Both Groups

Parameter	**Groups (Means ± SD)**		**P Value**	**Significance**
	Case Group (N-40)	Control Group (N-40)		
Age (yrs)	30.33 ± 3.28	29.65 ± 3.50	0.37	NS
Height (m)	1.62 ± 0.10	1.64 ± 0.11	0.39	NS
Weight (Kg)	56.33 ± 9.87	61.05 ± 14.84	0.098	NS
BMI (Kg/m^2)	21.51 ± 3.13	22.63 ± 4.21	0.192	NS

Table 1 shows Anthropometric parameters of Allergic Rhinitis (Case) group and Control group.
NS- Non significant

Table 2: HRV parameters of Both Groups

Parameter	**Groups (Means ± SD)**		**P Value**	**Significance**
	Case Group (N-40)	**Control Group(N-40)**		
LF (n.u.) %	44.77 ± 17.15	56.46 ± 16.12	0.044	**S***
LF (ms^2)	235.6 ± 159.1	314 ± 182.5	0.03	**S***
HF (n.u.) %	54.9 ± 17.16	43.39 ± 16.07	0.047	**S***
HF (ms^2)	263.4 ± 116.6	215.2 ± 96.4	0.02	**S***
LF/HF Ratio	1.01 ± 0.663	1.759 ± 1.407	0.005	**S***

Table 2 shows Comparison of HRV Parameters of Allergic Rhinitis (Case) group and Control group
[Abbreviations- HF- High Frequency, LF- Low Frequency, LF/HF- ratio of absolute LF to HF power, LF (n.u.) normalized low frequency, HF (n.u.) normalized high frequency]
S*- Significant

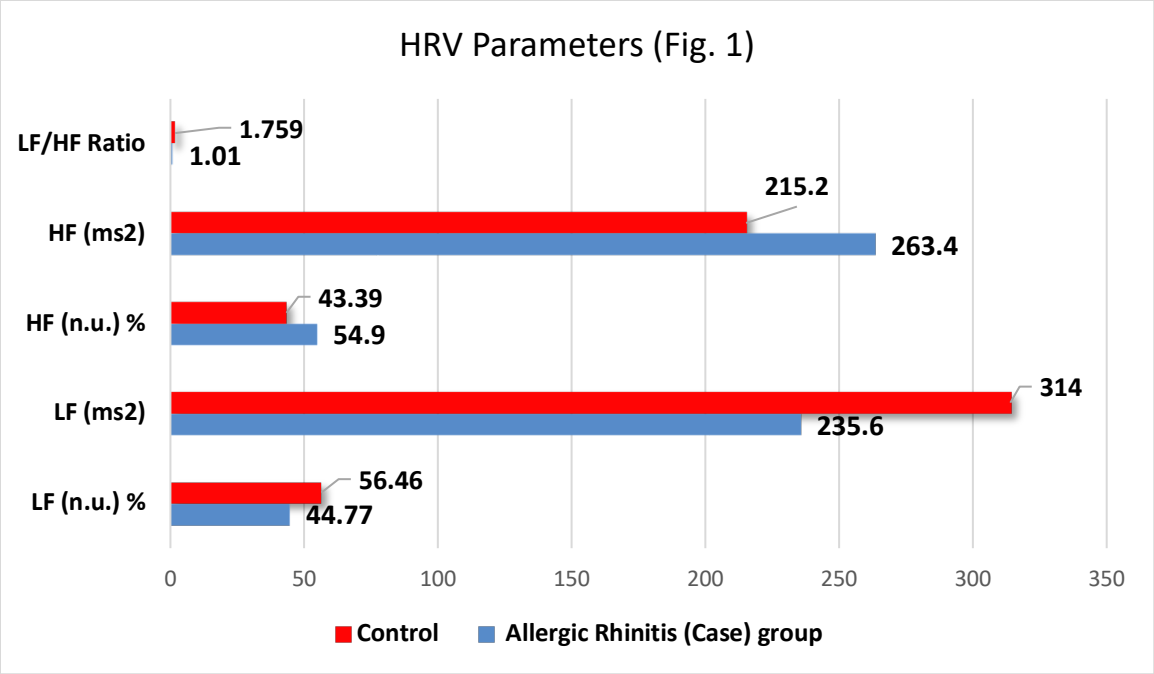

Figure 1: Comparison of HRV Parameters in Allergic Rhinitis (Case) group and Control group

[Abbreviations- HF- High Frequency, LF- Low Frequency, LF/HF- ratio of absolute LF to HF power, LF (n.u.) normalized low frequency, HF (n.u.) normalized high frequency]

Discussion

The present study was an effort to discover the degree of autonomic dysfunction in patients of Allergic Rhinitis. The important findings of this study were increased parasympathetic reactivity, as evidenced by the increased values of HF (ms^2) and HF (n.u.) [Table 2] whereas, blunting of sympathetic reactivity was evidenced by decrease values of LF (ms^2) and LF (n.u.) [Table 2], along with diminished Sympathovagal balance which evidenced by decreased LF/HF ratio.

The association between the ANS and inflammatory diseases have been revealed by many studies in the past. In these studies, Parasympathetic division was proposed as the major wing/part involved in the tuning of inflammatory reflexes that were postulated towards controlling innate immune responses.[14] Decreased vagal activity disrupts the innate immune regulation, causing continual proinflammatory cytokine activity and excessive or chronic inflammation.[15]

Ishman *et al*. (2007) [9] evaluated ANS function in patients with perennial AR measuring HRV and blood pressure responses to a broad battery of autonomic function. They found hypofunction in the sympathetic system whereas no dysfunction in parasympathetic system. Our study also showed similar results of sympathetic hypofunction. Tascilar E *et al* (2009) concluded after their study on pediatric patients of AR that HRV increased in these patient's which implicated Sympathetic withdrawal and Parasympathetic predominance.[10]

Boettger, M. K., *et al*,(2008) and D. Cicek, (2008) *et al*. both found similar results of sympathetic hypofunction and parasympathetic predominance in Atopic Dermatitis patients suggesting that there will

be increase parasympathetic and decrease sympathetic activity in Allergic diseases.[17,18] Similarly Lutfi MF,(2012) and Gupta J *et al*.(2012) concluded after their study on Asthmatic patients that there was significantly raised central parasympathetic outflow and a concomitant significantly low central sympathetic outflow in asymptomatic Asthmatic subjects as compared to that observed in control group.[19,20]

Emin O *et al* (2012) [11] performed a study that shows positive correlation between the disease severity in children suffering from AR and ANS dysfunctions. They observed strikingly abnormal patterns of autonomic functions in children suffering from AR and shown a significant association between ANS dysfunction as assessed by RR interval and prolonged SSR is related to the severity of the AR. Their results indicated that there will be increased parasympathetic activity in AR children.The results of our study also supported by Lan MY *et al* (2013) [21], and Kim M H *et al* (2016).[12] They both indicated that the parasympathetic nervous activity is predominant as well as sympathetic activity decreases in patients with AR.

The present study proposes a definite involvement of the ANS in patients with AR by demonstrating a statistically significant difference in the parameters of HRV tests by deploying a standardized HRV tests. The cardiovascular autonomic reactivity methods used in the present study indicates towards a compromised status of both sympathetic and parasympathetic division of the autonomic nervous system.

Conclusion

The findings of the present study indicate towards an enhanced reactivity of the parasympathetic division and a blunted reactivity of the sympathetic nervous system along with a blunted sympathovagal balance in patients with Allergic Rhinitis. The impaired status of ANS functioning puts Allergic Rhinitis patients at a greater cardiovascular risk warranting an early assessment of ANS functions. This could potentially prevent the overall morbidity in Allergic Rhinitis patients and might prove crucial in early detection and timely management of severe consequences of cardiac autonomic dysfunction such as Ischemic heart disease, Peripheral vascular disease, and Myocardial infarction.

Limitation

A small sample size precludes the direct extrapolation of the findings obtained in the present study onto the general population. Also, contextually, the present study refrained from classifying the disease further on the basis of its duration and severity and hence the results so obtained are only sufficient enough for making gross comparison of ANS dysfunction with apparently healthy normal controls.

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