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Full length Research Article

Association Between Spectral Analysis of Heart Rate Variability and Pulmonary Function Tests in Bronchial Asthma Patients

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Summary: The parasympathetic vagus nerve supplies the heart and lungs. The parasympathetic activity modifies the heart rate and force of contraction in the heart and bronchial smooth muscle constriction and hypersecretion of mucus in the lungs. There is a link between these two components. Hence, this study is designed to find the association between spectral analysis of heart rate variability and pulmonary function tests in bronchial asthma patients. In this study, 30 asthmatic patients were recruited from the respiratory medicine outpatient department and 30 healthy volunteers were also included. Pulmonary function tests and heart rate variability parameters were recorded in the physiology department. The pulmonary function parameters were found to be significantly reduced in the asthmatic patient and it shows obstructive lung diseases. Heart rate variability parameters showed a statistically significant decrease in mean HR, VLF ms^2, and LF ms^2 in the asthmatic patients when compared to controls. HF ms^2 was found significantly increased in the asthmatic patient. These HF ms^2 were increased to represent parasympathetic hyperactivity. This study concluded that there is parasympathetic dominance in asthmatic patients. The autonomic dysfunction increases parasympathetic active leads to airway bronchoconstriction and hypersecretion of mucus in asthmatic patients. There was a negative correlation found between the FEV1 value and HF ms^2.

Keywords*: HRV, Spectral analysis, Frequency analysis, PFT, Asthma, HF, LF*

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INTRODUCTION

According to a WHO (2019) report, asthma is affected 262 million people and 4,55000 deaths have been documented worldwide. Asthma constitutes 1% of the global disease burden. In India, nearly 15-20 million people were affected by asthma. Asthma prevalence is higher in high-income countries and most asthma-related deaths occur in low-middle-income countries (Dharmage *et al*., 2019). The prevalence of diseases is rising throughout the huge nation of India as a result of factors like population density, climatic conditions, socioeconomic and educational position, industrialization, congested traffic, and the number of automobiles. All age groups are affected by this serious non-communicable disease, which is characterized by a persistent cough, wheezing, and tightness in the chest. Asthma is a reversible airway constriction and inflammation in response to infection, environmental allergens, and irritants (Patel *et al*., 2019). Bronchial asthma is associated with positive family history hence genetic history is a predisposing factor in the development of asthma. Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play an important role (Yawn *et al*., 2005). It is also associated with allergy and elevated plasma IgE levels.

Asthma cannot be cured, although the symptoms can be relieved by medications like inhalational corticosteroids and β agonists used for quick relief medication (Patel *et al*., 2019). In the lungs, Airway smooth muscle is innervated by sympathetic and parasympathetic nerve fibers. The stimulation of sympathetic nerves causes relaxes airway smooth muscles producing bronchodilatation. The parasympathetic stimulations lead to airway smooth muscle constriction leading to bronchoconstriction. Both the two autonomic limbs have to act in a balance to maintain an optimal airway luminal diameter (Canning *et al*., 2001). In bronchial asthma was found that autonomic dysfunction and hyperactivity of the cholinergic parasympathetic system are responsible for bronchoconstriction and hypersecretion of mucus (de Freitas Dantas Gomes *et al*., 2015). The parasympathetic vagus nerve controls the lungs and heart. Parasympathetic dominance is also reflected in heart rate.

Heart rate variability (HRV) is the most sensitive indicator of autonomic functions and assessment of sympathovagal balance (Fournié *et al*.,2021). There is an association between variations in beat-to-beat heart rate and bronchial airway changes. Hence this study is designed to find the association between spectral analysis of heart rate variability and pulmonary function tests in bronchial asthma patients.

MATERIALS AND METHODS

This is an analytical cross-sectional study design conducted in the department of physiology, PSG Institute of Medical Sciences and Research in Coimbatore Tamil Nadu, India. This study was approved by the Institutional Human Ethics Committee according to the Declaration of Helsinki. (Proposal No.12/178) The study procedure was explained to the patients and healthy volunteer controls. A total of 60 participants of which 30 asthmatic patients and 30 healthy volunteer controls were recruited from age groups between 20 and 45 years. We selected the patient from the outpatient department of the respiratory medicine department in PSG hospital. We only included research participants who were willing to provide written consent. The patients were selected based on their clinical history of cough, wheezing, chest tightness, dyspnea and FEV1 value. the further present history of illness and treatment details were obtained. We excluded patients with other diseases like hypertension, diabetes, thyroid disorders, ischemic heart disease & myocardial infarction. Smokers, alcoholics and pregnant women also were excluded from our study. Normal healthy volunteers in the same age group are recruited as controls. General physical examinations including height and weight were recorded. Participants were instructed to have a light meal and good sleep the previous night. Before the procedure participants are advised to avoid exercise and caffeinated drinks for 24 h.

Pulmonary function tests and heart rate variability were recorded in the morning 9.00 – 12.00 AM. In a standing position, pulmonary function tests (PFT) were recorded by using Spiropalm-digital spirometry. Ask the subject to breathe normally and then close their nostrils to inhale fully and exhale the air rapidly and forcefully with maximal effort. Repeat for a minimum of three times, Check FEV1 and FVC repeatability (Graham *et al*., 2019). The parameters of PFT taken in the study are forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), FEV_1/FVC ratio, peak expiratory flow rate (PEFR), and $FEF_{25-75\%}$ parameters obtained.

Heart Rate Variability (HRV) is a non-invasive procedure. An electrocardiograph recording was done by using a computerized physiograph (NEVIQURE- Digital ECG recorder). Before HRV recording to avoid anxiety ask the subject to sit silently for a few minutes in the physiology research laboratory. We prefer short–term recording of HRV, it is feasible for research and clinical interpretations. According to the recommendation task force guidelines, short-term (5 min) recording covers the entire spectral analysis. (Nunan *et al*., 2010).

The spectral or frequency domain analysis oscillations of the heart rate signal, Separate the different frequencies and amplitudes and provides information on how power distributes as a function of frequency. This provides information about estimating the degree of sympathetic and parasympathetic balances (Franco *et al*., 2020). The Lead II ECG was recorded in the supine position for 5 minutes with the use of adhesion electrodes in both wrists and legs. After recording the baseline HRV from the study participants, RR intervals were isolated by the digital filtering of noise and baseline fluctuation. When patients with abnormal ECG findings like ectopic beats, were dropped from the study group. Data filtering was done by digital notch filters at a rate of 1000 samples per second. RR interval peaks were recorded as time points (Pichon *et al*., 2005).

Frequency domain analysis was done after the careful exclusion of abnormal heartbeats and artifacts. The frequency domain parameters Low Frequency (LF ms^2), Low Frequency normalized units (LF n.u), High Frequency (HF ms^2), High Frequency normalized units (HF n.u), Very Low Frequency (VLF ms^2)and LF/HF power ratio were obtained. Kuopio software was used to analyze the harmonic components of the RR interval.

Statistical analysis

SPSS 19 software was used for statistical analysis. An independent Student's t-test was used to compare the study group and control group. Pearson correlation analysis was used to correlate FEV_1% and HF ms^2. The Chi-Square test was used to link the family history of bronchial asthma.

RESULTS

In this study, pulmonary function tests and frequency domain HRV were recorded there is no significance in the physical parameters like age, height, weight and BMI (Table1).

Table 1
Physical characteristic of asthmatic patients and healthy controls are compared**.**

Parameters	Asthmatic patients (30)	Controls (30)	P. value
Age (years)	32.03 ± 8.52	31.27 ± 7.08	0.708 (NS)
Weight (kg)	60.8 ± 11.62	62.4 ± 12.09	0.603 (NS)
Height (cm)	162.93± 9.56	161.53±11.07	0.602 (NS)
BMI (kg/m^2)	23.05 ± 3.19	23.89 ± 2.85	0.286 (NS)

NS – Not significant

As shown in Table 2, all pulmonary function parameters were FVC, FEV1, FEV1/ FVC%, FEF 25-75%, and PEFR (p. Value < 0.0001) seen as statistically significantly reduced in asthmatic patients when compared to the controls.

Table 2
Comparison of pulmonary function parameters between asthmatic patients and controls

Pulmonary function Parameters	Asthmatic patients (30)	Controls (30)	P. value
FVC (L)	2.29 ± 0.70	3.65 ± 0.82	< 0.001 *
FEV_1 (L)	1.56 ± 0.59	3.11 ± 0.69	< 0.001 *
FEV1/FVC %	63.74 ± 7.9	84.82 ± 1.92	< 0.001 *
$FEF_{25-75\%}$ (L)	1.08 ± 0.5	3.43 ± 0.42	< 0.001 *
PEFR (L/sec)	3.75 ± 1.79	7.69 ± 1.25	< 0.001 *

**significant AP – Asthmatic patients, C – controls*

Table 3 shows, Mean HR was decreased in the asthmatic patients when compared to controls (P<0.001). Frequency domain parameters HF(ms^2) shows there was a significant increase in asthmatic patients (P<0.001). There is a significant decrease in LF(ms^2), LF/HF and VLF (ms^2) ratio (P<0.001) values among asthmatic patients. The further finding showed there was a reduction in LF n.u and an increase in HF n.u among asthmatic patients which was not significant.

Only HF(ms^2) found a significant negative correlation with FEV1% with an r value < 0.05 which shows the decrease in FEV_1% increases HF. No significant correlation was not found in other parameters. Those who had a family history of bronchial asthma had a 45-fold higher risk of developing asthma, according to research linking family history with bronchial asthma.

Table:3
HRV frequency domain parameters compared with asthmatic patients and controls

HRV Frequency domain parameters	Asthmatic patients (30)	Controls (30)	P value
Mean Heart Rate	74.73 ± 6.97	83.23 ± 8.7	< 0.001 *
High Frequency (HF) ms^2	143.23 ± 25.46	85.9 ± 11.18	< 0.001 *
Low Frequency (LF) ms^2	199.4 ± 35.27	331.07 ± 64.27	< 0.001 *
Low Frequency (LF) n.u	68.89 ± 11.82	69.19 ± 9.72	0.941 NS
High Frequency (HF) n.u	33.47 ± 15.79	30.78 ± 9.72	0.430 NS
LF/HF ratio	1.66 ± 0.24	3.85 ± 0.37	< 0.001 *
Very Low Frequency (VLF) ms^2	1289.36 ± 285.89	2334.23 ± 520.20	< 0.001 *

n.u** - normalized units* * - Significant, NS - Not significant***

DISCUSSION

The present study suggested autonomic dysfunction in bronchial asthmatic patients. Pulmonary function tests showed obstructive lung diseases. This decreased FVC in asthmatics is due to increased residual volume and decreased lung compliance. This was attributed to increased cholinergic parasympathetic stimulation which causes bronchoconstriction and air trapping causing increased residual volume. FEV_1, FEV_1/FVC, FEV_{25-75}% and PEFR were also decreased in the asthmatic patients due to bronchoconstriction and hypersecretions as a result of increased cholinergic parasympathetic stimulation. Decreased FEV_{25-75} % suggest the presence of small airway obstruction (Gallucci *et al*., 2019, Campbell *et al*., 2006). This enhanced parasympathetic and attenuated sympathetic activity will aggravate bronchoconstriction of the respiratory tree and consequently worsen airway narrowing. (Lutfi *et al* ., 2015 b)

The decreased mean HR interval in asthmatic patients shows that there is an increase in the parasympathetic vagal tone (Gupta *et al*., 2012). Parasympathetic vagal stimulation releases the neurotransmitter acetylcholine which inhibits the sinoatrial (SA node) node slowing down the heart rate.

LF (ms^2) and LF n.u in normalized units both are denoted sympathetic mediated HRV. LF(ms^2) was statistically significantly reduced in asthmatic patients (Garrard *et al*.,1992). The LF n.u decreased in asthmatic patients but no statistically significant difference was found This suggested that sympathetic tone was decreased in asthmatic patients.

HF(ms^2) and HF n.u denote parasympathetically mediated HRV. The individuals with asthma had statistically higher HF(ms^2) levels. However, there was no statistically significant increase in HF (nu) in asthmatic patients. It was implied that the parasympathetic tone had increased. Inspiration is predominantly suppressed by the parasympathetic vagal system when the cardiovascular center receives an impulse from the medullary respiratory system. (Lutfi *et al*., 2012 a, Ostrowska-Nawaryez *et al*., 2006, Du J *et al*., 2001 and Fujii *et al*., 2000).

LF/HF ratio was statistically decreased in asthmatic patients when compared to controls. The LF/HF ratio denotes sympathovagal balance. Decreased LF/HF ratio in asthmatics patients increased parasympathetic dominance (Gupta *et al*., 2012).

A substantial negative correlation was found between HF(ms^2) and FEV1%. The HF(ms^2) heart rate fluctuations raise caused a reduction in FEV1%. This shows that asthma enhanced the parasympathetic tone.

Environmental variables can be avoided, but genetic predisposition cannot be changed. Planning preventative measures to address environmental risk factors might be aided by knowledge of a family history of bronchial asthma. Without treatment, asthmatic episodes can significantly lower the quality of life by interfering with daily activities including sleep, study, work, and exercise.

In conclusion, the patients with asthma showed the predominance of parasympathetic activity. The autonomic dysfunction is increased by central parasympathetic activity from the medullary respiratory center leading to airway bronchoconstriction and hypersecretion of mucus caused by an obstruction in the airways of asthmatic patients. It was shown that there was a negative correlation between the FEV1% and HF (ms^2) value.

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