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A Comparative Study of Heart Rate Variability in Smokers and Non Smokers.

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ABSTRACT

Smoking is an escalating public health problem especially in developing countries like India. It is a major risk factor for coronary artery diseases, cerebrovascular stroke, peripheral vascular diseases. Studies have shown that smoking increases the risk of myocardial infarction and sudden cardiac death. One of the mechanism by which smoking impairs the cardiovascular function, is its effect on Autonomic Nervous System control. There are several tests to determine the autonomic activity. Recently the most accepted tool is determining Heart Rate Variability. This study intends to evaluate the autonomic functions in cigarette smokers and non smokers. This is a case control study having a total of 100 male subjects – 50 cigarette smokers (cases) and 50 non smokers (controls) in the age group of 25-35 years. Electrocardiography (ECG) was recorded in a quiet room with the subject in supine position after 10 minutes of rest. Analog ECG signal was converted to digital. Following parameters were taken – SDNN,RMSSD, pNN50, E:I ratio, LF(nu), HF(nu), LF/HF. Results were compared with the help of Student t test and the level of significance was fixed at $p < 0.05$.There was significant decrease in SDNN ($p<0.001$), RMSSD (<0.001), pNN50 (<0.001), E:I ratio ($p<0.001$), HF ($p<0.001$) and significant increase in LF ($p<0.001$), LF/HF ($p<0.001$) in cases when compared to controls. This signifies higher sympathetic activity and decreased parasympathetic activity in smokers when compared to non smokers. The present study showed that cigarette smoking in males may affect the cardiac autonomic activity. There was a ift in the sympathovagal balance towards sympathetic predominance among cigarette smokers when compared to non-smokers.

Keywords: Heart rate variability, SDNN, RMSSD, p NN50, LH nu, HF nu

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INTRODUCTION

Smoking is an escalating public health problem especially in developing countries like India [1]. The World Health Organization's (WHO) report on the Global Tobacco Epidemic in 2008 highlighted that approximately 5.4 million deaths every year are related to tobacco use. Unchecked that number will increase to more than 8 million a year by 2030. Tragically, with more than 80% of those deaths occurring in the developing world making it more relevant in our part of the world [2].

Smoking is a major risk factor for coronary artery diseases, cerebrovascular stroke, peripheral vascular diseases [3] and there is a general agreement that smoking increases the risk of myocardial infarction and sudden cardiac death [4]. Harmful effects of smoking appear at an early age, seriously affecting the brain, cardiovascular system, gastrointestinal system, immune functioning, and the respiratory systems [5]. Cessation of smoking is associated with reduced cardiovascular mortality and morbidity [6]. In India, smoking is less prevelant among females and for majority of whom it is also a taboo. So in the present study, we have included only male smokers.

Imbalance in cardiac autonomic activity might be a predisposing factor for arrhythmogenesis and subsequently sudden cardiac deaths [7]. Cigarette smoking increases the risk of cardiovascular events related with several mechanisms. One of the mechanism by which smoking impairs the cardiovascular function is its effect on Autonomic Nervous System [8]. There are several tests to determine the cardiac autonomic activity. Recently the most accepted tool is determining Heart Rate Variability (HRV) [9]. Therefore the present study was undertaken mainly to assess the effect of cigarette smoking on cardiac autonomic function using HRV.

Heart Rate Variability is a specific and sensitive noninvasive tool to evaluate cardiac autonomic activity. HRV is the degree of variation of the heart rate during the day under the balanced influence of sympathetic and parasympathetic component of the cardiac autonomic nervous system. It expresses the total amount of variation of both instantaneous heart rate and RR intervals. HRV also indicates the extent of neuronal damage to autonomic nervous system.

HRV has been shown to be a good tool to quantify the tone of autonomic nervous system to the myocardium. It has also been associated with high predictive value in many diseases where a disturbance in the autonomic activity is likely.[10-12]

This study is an effort to assess the cardiac autonomic activity using Heart Rate Variability in smokers.

MATERIALS AND METHODS

This study was conducted in Sri Siddhartha Medical College and Hospital, Tumkur. This is a comparative study having 50 male cigarette smokers in the age group of 25-35 yrs, smoking a minimum of 5 cigarettes per day for atleast 5 years[3] as cases and 50 age, BMI and sex matched non smoker subjects as controls (table 1 & 2). Clearance for the study protocol was obtained from institutional ethical committee. Subject's clinical history and details were taken according to the standard proforma. Informed written consent was taken from all the study subjects. The study involved non-invasive procedures and was performed at room temperature.

Subjects with history of major illness like diabetes mellitus, hypertension, chronic respiratory illness, cardiac diseases and endocrinal disorders, subjects on any drugs affecting the functioning of Autonomic Nervous System- like alpha blockers , beta blockers and others which might have an effect on the Autonomic Nervous System and with BMI >25 kg/m^2 were excluded from the study.

Experimental design

Weight and height were measured using standard calibrated instruments. Procedure was done between 9:00 AM to 12:00PM. All the subjects abstained from meals, alcohol or caffeine-containing beverages& any energetic physical activity for 4 hours prior to the examination, while smokers were asked not to smoke for 8 hours at least prior to the examination. Patient was explained in detail about the ongoing procedure and ECG was digitally recorded.

- ECG machine (BPL Cardiart 1087/MK-V) was used to acquire the analog ECG signal from the subject.
- Analog to digital converter (National Instruments NI-DAQ 7.5 USBD 6008) was used as the hardware, which converted the analog to digital signal and processed it to the computer with the help of the NI-DAQ software.
- Heart Rate Variability software (version 1.1), was used in the computer, to detect the peak to peak intervals and further mathematical and analytical calculations in order to get the values of the parameters.

The patient was made to lie down for 10 minutes and allowed to relax and then the limb electrodes were placed on to the respective limbs along with ECG gel. The chest leads were not used & ECG was recorded in lead II only, as the requirement for the procedure was only peak detection for the determination of RR intervals. First, a 5 minutes ECG in supine position was recorded, with subject respiring normally. This was used to determine the SDNN (Standard Deviation of Normal to Normal RR intervals expressed in milliseconds (ms) mainly signify parasympathetic component), RMSSD (Square root of the mean of the sum of the squares of differences between adjacent NN intervals) , pNN50(percent of differences between adjacent NN intervals that are greater than 50ms) [10], LF nu (Low Frequency component, where nu means statistically normalized units. This mainly signify sympathetic component), HF nu (High Frequency component This signify parasympathetic component) and LF/HF (Ratio of Low Frequency component to High Frequency component which signify the sympathovagal balance.). Then, the person was periodically instructed to take alternating 5 seconds of deep inspiration and 5 seconds of deep expiration for a period of 2 minutes and simultaneous ECG was recorded. This data was used to measure the E/I ratio (Expiratory RR interval to Inspiratory RR interval ratio which mainly signify parasympathetic component.) [9].

Statistical analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented. Significance was assessed at 5 % level of significance (p value <0.05). Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters in Number (%).

Significant figures

+ Suggestive significance (p value: $0.05<p<0.10$)
* Moderately significant (p value:$0.01<p \leq 0.05$)
** Strongly significant (p value : $p \leq 0.01$)

Statistical software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

The major findings of this study were, there was a significant reduction in the values of SDNN, RMSSD, pNN50, E:I ratio, HF nu in smokers ($p< 0.001$) when compared to non smokers. Also there was a significant increase in the values of LF nu and LF/HF ratio in smokers ($p< 0.001$) when compared to non smokers.

Table 1: Age distribution of subjects studied

Age in years	Cases (50)		Controls (50)	
	No	%	No	%
25-30	41	82.0	43	86.0
31-35	9	18.0	7	14.0
Total	50	100.0	50	100.0
Mean ± SD	28.62±2.39		28.10±2.53	

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Table 2: Comparison of BMI and Waist Hip ratio between cases and controls

	Cases	Controls	p value
BMI (kg/m2)	22.75±1.73	23.19±1.31	0.157
Waist Hip Ratio	0.841±0.03	0.844±0.03	0.482

Table 3: Comparison of Time domain parameters between cases and controls.

HRV	Cases	Controls	p value
SDNN(ms)	34.22±14.00	69.10±26.09	<0.001**
RMSSD(ms)	28.61±16.03	76.47±44.17	<0.001**
PNN50 %	7.78±10.71	35.68±19.20	<0.001**
E/I ratio	1.37±0.14	1.76±0.46	<0.001**

Figure 1: Comparison of SDNN between cases and controls

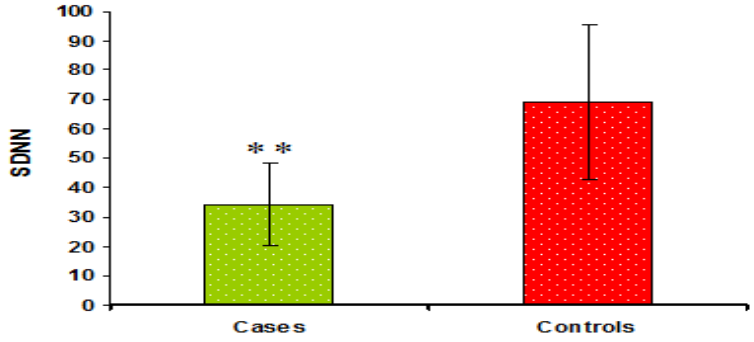


Figure 2: Comparison of RMSSD and pNN50 between cases and controls

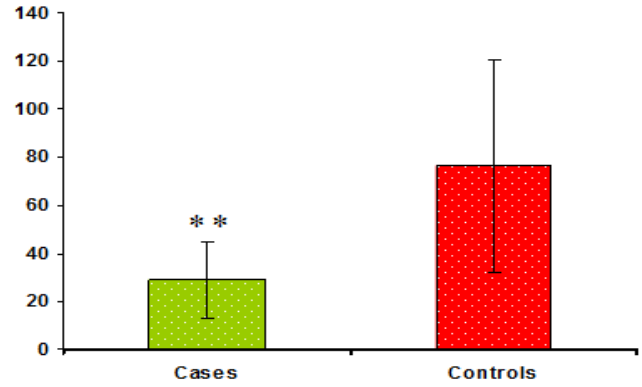
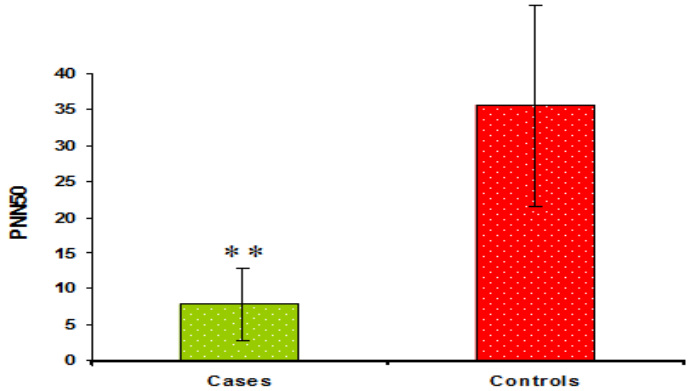


Figure 3: Comparison of E:I ratio between cases and control



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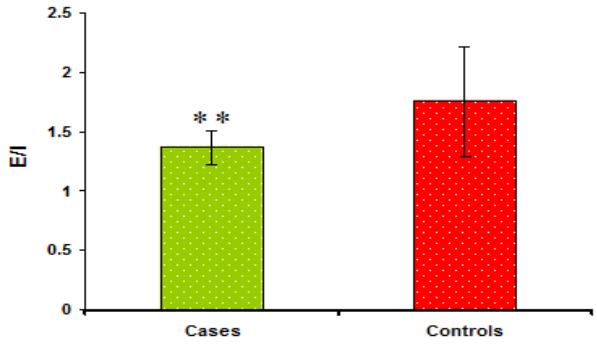


Table 4: Comparison of Frequency domain parameters between cases and controls.

HRV	Cases	Controls	p value
LF nu	61.52±14.62	36.11±11.68	<0.001**
HF nu	38.49±14.64	63.70±11.97	<0.001**
LF/HF	2.10±1.54	0.63±0.36	<0.001**

Figure 4: Comparison of LF nu between cases and controls.

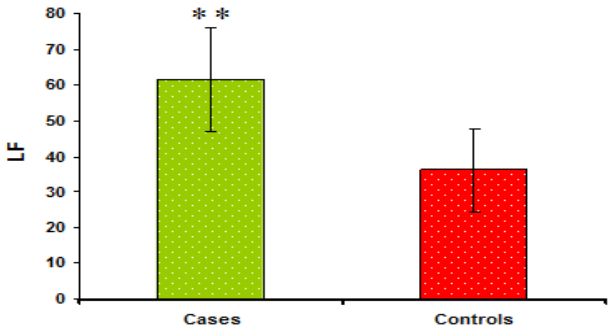


Figure 5: Comparison of HF nu between cases and controls

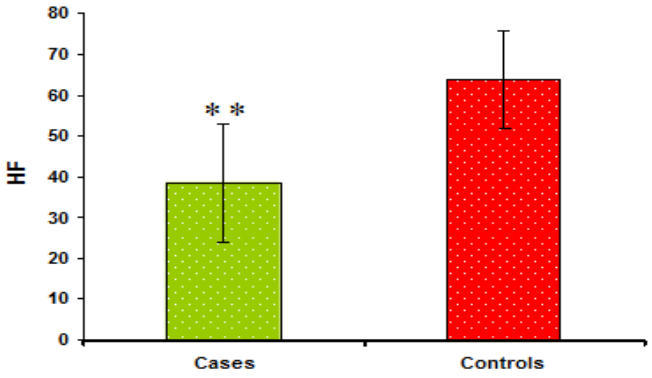
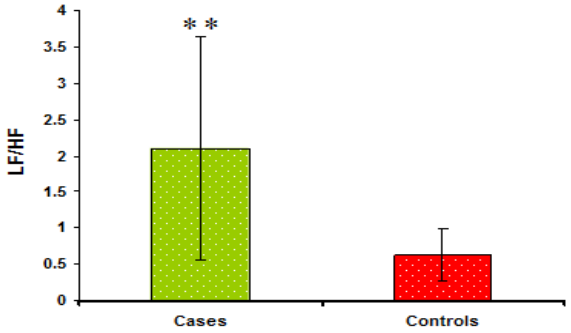


Figure 6: Comparison of LF/HF ratio between cases and controls



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DISCUSSION

This study was designed to evaluate the autonomic function in cigarette smokers and non smokers using HRV. All the study subjects were age, BMI and WHR matched.

In the present study the following HRV parameters were estimated – Time domain parameters like SDNN, RMSSD, p NN50 and E/I ratio, frequency domain analysis parameters like LF nu, HF nu and LF/HF in smokers and non smokers in the age group of 25-35 years.

The major findings of this study were, smokers showed significant reduction in the values of SDNN, RMSSD,Pnn50, E:I ratio, HF nu which are considered as a measure of parasympathetic activity and showed a significant increase in the values of LF nu (which is considered as a measure of sympathetic activity) and LF/HF ratio (which signifies the sympathovagal balance)when compared to non-smokers.

This observation is in agreement with experimental data which showed that smoking resulted in acute modifications in the HRV indices, characterized by a decrease in the parasympathetic activity and increase in the sympathetic activity [13].

Furthermore, it has been shown that Smoking impairs the sympathovagal balance and increases the hs-CRP activity in otherwise healthy smokers, the combination of which would probably contribute to a higher rate of cardiovascular events [14].

The observed sympathetic excitatory effect in cigarette smokers is in accordance with earlier studies ascribing similar powerful Sympathetic excitatory effect in smokers, influencing sympathetic drive to muscle blood vessels, to skin, and to the heart [15].

As for as the mechanisms responsible for the sympathoexcitatory effects are concerned, Shinozaki N, et al. showed that in healthy subjects, cigarette smoking has been found to increase HR, BP, and the plasma concentration of norepinephrine. These changes are attenuated markedly by alpha-adrenergic and beta-adrenergic blockade, indicating that these hemodynamic effects of cigarette smoking are derived from sympathetic activation. However, the mechanisms of cigarette smoking-mediated sympathoexcitation are unclear.

They assume 3 different mechanisms underlying activation of the sympathetic nervous system due to cigarette smoking. First, a direct effect on the central nervous system; second, a stimulatory effect on ganglionic sympathetic transmission that leads to a subsequent increase in postganglionic efferent sympathetic nerve activity; and third, a direct effect on peripheral sympathetic nerve endings. It has been shown that cigarette smoking stimulates the release of catecholamine directly from postganglionic peripheral sympathetic nerve endings. However, the mechanism of the effect of cigarette smoking on the central nervous system is still controversial [16].

Thus, our study proves that there is strong impairment of parasympathetic activity with elevated levels of sympathetic activity in healthy smokers when compared to non smokers. And this has led to definite shift in the sympathovagal balance towards sympathetic component.

Therefore smokers are prone for cardiovascular risk. So encouraging abstinence from smoking, in early stages can revert back the cardiovascular changes to nearly normal or in more severe cases to recovery with little residual damage to the heart.

CONCLUSION

In this study, HRV parameters i.e. Frequency domain and Time domain were compared between 50 non smokers and 50 smokers. At the end of the study, the following conclusions can be drawn.

- There was a demonstrable decrease in parasympathetic activity in smokers when compared with age and BMI matched non smokers.

- There was also a demonstrable increase in Sympathetic activity in smokers when compared with age and BMI matched non smokers.
- An increase in sympathetic activity and decrease in parasympathetic activity tilted the balance of autonomic functions to sympathetic predominance among the smokers.

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