Original Research Article **Physiology**

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

STUDY ON CARDIAC AUTONOMIC MODULATION WITH THE SEVERITY OF METABOLIC SYNDROME

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ABSTRACT

Metabolic syndrome is a cluster of interconnected risk factors for cardiovascular disease which includes obesity, diabetes, hypertension and dyslipidemia. Heart rate variability is used to detect cardiac autonomic dysfunctions. Objective of the study is to compare the cardiac autonomic modulation by Time – Domain parameters of HRV with the metabolic syndrome and its severity. A total of 195 patients were divided into 3 groups as group I with those having only 3 components of the metabolic syndrome, group II with more than 3 components of the metabolic syndrome and group III with less than three components of the metabolic syndrome. The group I served as normal MS people, the group II as severe MS and group III as control group. The Time-domain HRV parameters like mean HR, mean RR, RMSSD, NN50 and pNN50 were recorded in those subjects and were analyzed by ANOVA. The result showed that group II had high mean HR values and low RMSSD values than group I and group III. Mean HR and RMSSD parameters of group II and group III were comparable. Mean RR values of group II showed less value which was comparable between group I and II and group II and III. NN50 and pNN50 values showed no significant ($p = 0.08$) difference across the groups. Metabolic syndrome increases the sympathetic activity and decreases the parasympathetic activity causing abnormal cardiac autonomic control and it is proportionate with severity of metabolic syndrome. HRV can be used as a screening and diagnostic tool for metabolic syndrome population.

KEY WORDS: *Metabolic syndrome, cardiac autonomic modulation, Time – domain, HRV.*

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Received on: 15-05-2017
Revised and Accepted on: 19-06-2017
DOI: http://dx.doi.org/10.22376/ijpbs.2017.8.3.b665-668

INTRODUCTION

The metabolic syndrome (MS) is a complex of interrelated risk factors for cardiovascular disease (CVD) and diabetes, which includes dysglycemia, raised blood pressure, elevated triglyceride levels, low high–density lipoprotein, cholesterol levels and central obesity.[1] The metabolic syndrome is associated with the development of diabetes and increases the cardiovascular disease (CVD) events, including atrial fibrillation, acute coronary syndrome, cardiac death and overall mortality.[2] Worldwide, it affects 10 to 25 percent of adult population.[3] Heart rate variability (HRV) is a non – invasive test which is used to detect the cardiac autonomic functions and it predicts mortality from cardiovascular disease.[4] Time–domain is based on statistical operation on R – R intervals which consists of mean Heart Rate [HR] per min, mean RR interval in sec., Root mean square of successive differences [RMSSD] in msec., Number of pairs of successive NNs that differ by more than 50ms [NN50] in count, proportion of NN50 divided by total number of NNs [pNN50] in %. Decrease of all the above parameters reflects poor parasympathetic activity and better sympathetic activity.[5] Cardiac autonomic dysfunction might be the pathophysiology behind metabolic syndrome. Although many attempts have been done to study the cardiac autonomic functions with individual component of metabolic syndrome, the relationship between the metabolic syndrome and its severity with cardiac autonomic functions in Indian population is not available in the literature. Hence, the present study is conducted to find out the relationship between cardiac autonomic functions with metabolic syndrome and its severity. Objective of the study is to compare the cardiac autonomic modulation by time – domain parameters of HRV with the metabolic syndrome and its severity.

MATERIALS AND METHODS

The study was carried out in the department of Physiology, A C S Medical College and Hospital, Chennai. The participants were from A C S Medical College and Hospital, Saveetha Medical College and Hospital, Chennai. The study commenced after getting the approval from the Institutional Human Ethical Committee (IHEC), IHEC No. 005/12/2014/IEC/SU Saveetha University, Chennai. Data were collected from the participants after giving detailed explanation about the procedure and their cooperation and willingness was obtained with written informed consent. The study was conducted from January 2015 to June 2016. Sample size was calculated based on prevalence of metabolic syndrome in Chennai. The Prevalence of metabolic syndrome is 46.3% in Chennai.[6] The cross – sectional study was carried out among 195 subjects in three groups, each comprising 65 subjects. Age and sex matched subjects were recruited for the study. Group I: Subjects with any three components of metabolic syndrome (normal MS group) Group II: Subjects with more than three components of metabolic syndrome (severe MS group) Group III: Subjects with less than three components of metabolic syndrome (Control group) The diagnosed metabolic syndrome patients were recruited for the present study. The diagnostic criteria for metabolic syndrome were according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria (≥3 of 5 risk factors) and with the inclusion and exclusion criteria as detailed below.[1]

Inclusion criteria

Subjects with –

- Waist circumference ≥ 102cm (40 inches) in men and ≥ 88cm (35 inches) in women.
- Triglyceride ≥ 150 mg/dl or history of drug consumption for hypertriglyceridemia.
- HDL ≤ 40 mg/dl in men and ≤ 50 mg/dl in women or history of drug consumption.
- Systolic BP ≥ 130mmHg and diastolic BP ≥ 85mmHg or history of antihypertensive drug consumption.
- Fasting blood glucose ≥ 100 mg/dl, history of diabetes mellitus or using antidiabetic drug.

Exclusion criteria

Patients who were not willing to give the consent, pregnant women, patients suffering from neurological defect, patients suffering from urological defect, patients having cancer, patients with acute coronary syndromes within 3 months, patients with atrial fibrillation, subjects with past/present history of RS, CVS disorders.

Data collection

A detailed clinical history of all the subjects was taken. Relevant past history, family history, any drug history, personal history like smoking, alcoholism etc was taken. ECG recording was taken for 5 minutes after 10 minutes of seated rest, under standardized conditions to minimize artifacts. ECG signal was obtained using limb lead II and analysis was performed using HRV analysis software version 1.1, Biomedical Signal Analysis Group, Department of Applied physics, University of Kuopio, Finland. The recording was done in the morning hours between 9AM and 11 AM. The subjects were instructed to avoid coffee or alcohol 24 hours and food two hours prior to testing. While recording, the subjects were instructed to close the eyes, and to avoid talking, coughing, moving of hands, shaking the legs and body, and sleeping during the test.[6]

Statistical analysis

Statistical analyses were performed between the groups using SAS 9.2 version. All the variables were analysed by a non – parametric test called Kruskal Wallis test is used when the variable is not normally distributed across the groups. Wilcoxon – Mann – Whitney test is used to compare within the groups. Statistical significance is considered if the p – value is less than 0.05.

RESULT

Participants were between 30 – 60 years. Among the Time – domain parameters of HRV, when compared between the groups (table 1), the value of mean HR in group II (83.30 ± 12.20) was significantly high ($p<0.008$) with that of group III (76.82 ± 13.22) whereas the mean HR values of Group I (80.23±12.52) with Group II and Group I with Group III (76.82 ± 13.22) were not

statistically significant. But the RMSSD of group II (22.46 ± 22.32) was significantly different (p<0.009) when compared with that of the group III (32.09 ± 27.21) and not with the group I (26.28 ± 21.67). The RMSSD values between the Group I and III and Group I and II did not show statistically significant difference. Among the groups, the mean RR interval showed less in group II (0.65 ± 0.08) which was significant (p<0.0001) when compared with that of group I (0.70 ± 0.09) and also group III (0.73 ± 0.08) though the mean RR of group I & III were not different between the groups. Incidentally, the time domain HRV values of NN50 and pNN50 showed no significant difference across the groups.

Table 1
Comparison of Time – Domain Parameters of HRV in different study groups (values expressed in mean ± SD)

Variables	Normal MS (Group I)	Severe MS (Group II)	Control (Group III)	F - Value	λ^2 - Value	P – Value, S
Mean HR (/min)	80.23 ± 12.52	83.30 ± 12.20	76.82 ± 13.22	4.90	---	P<0.008 * (GII&III)
Mean RR (s)	0.70 ± 0.09	0.65 ± 0.08	0.73 ± 0.08	16.38	---	P <0.0001** (both GI&II and GII&III)
RMSSD (ms)	26.28 ± 21.67	22.46 ± 22.32	32.09 ± 27.21	---	9.27	P<0.009* (GII&III)
NN50 (count)	12.53 ± 15.51	7.2 ± 11.90	14.45 ± 20.56	---	5.04	0.08 [NS]
pNN50 (%)	10.08 ± 13.33	5.39 ± 10.00	12.42 ± 19.02	---	5.04	0.08 [NS]

**** - Significant; ** - Highly significant; NS – Not significant***

DISCUSSION

Treatment of metabolic syndrome involves invasive, costly and time – consuming procedures. On the other hand, HRV is a simple, non – invasive procedure to detect the cardiac autonomic function of the subjects, which can be adopted at clinics for the diagnosis of metabolic syndrome. Hence, the present study aimed to compare the cardiac autonomic modulation by time – domain parameters of HRV with metabolic syndrome and its severity. The decrease in Time – Domain parameters of HRV indicates increased sympathetic activity. In the present study, the severe MS group showed significantly lower mean RR, RMSSD and also NN50 and pNN50 parameters though the later two parameters decrease was not statistically significant. Also with increase in mean HR recorded in severe MS group clearly indicate the occurrence of increased sympathetic activity which is proportionate with the severity of the disease. Researchers have studied correlation between HRV in time domain parameters and the main cardiovascular risk factors and have shown lower values of SDNN, mean RR, RMSSD, and pNN50 with increased mean HR which was in agreement with the present study.[8] Researchers have recorded short – term HRV for 5 minutes and demonstrated that in healthy adults, subjects with metabolic syndrome showed decreased SDNN and RMSSD when compared with subjects without metabolic syndrome, which is in agreement with the result of the present study.[4] Studies done on general population also have shown that subjects with MS had decreased SDNN compared to subjects without MS, which supports the result of the present study. [9-10] On contrary to these results, some researchers showed no differences in time – domain parameters of HRV in subjects with MS compared to subjects without MS.[11] Whereas, another study reported that HRV showed decreased SDNN in males with MS compared to males without MS.[12] Thus, the result of the present study clearly shows that the parasympathetic activity is decreased with increase in sympathetic activity proportionate to the severity of MS.

CONCLUSION

Metabolic syndrome unfavorably affects the cardiac autonomic function by causing sympathovagal imbalance with augmented sympathetic activity and worsening of parasympathetic activity. Time – domain parameters of HRV can be used as a screening and diagnostic tool, which helps in the management of metabolic syndrome. Further, longitudinal studies are required to validate the results of the present study.

CONFLICT OF INTEREST

Conflict of interest declared none.

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We sincerely thank the above reviewers for peer reviewing the manuscript