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RESEARCH ARTICLE

Autonomic functions in metabolic syndrome in Indian subpopulation using heart rate variability – A pilot study

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ABSTRACT

Background: The global industrialization and sedentary lifestyle has led to rise in obesity, hypertension, and diabetes which is associated with increased prevalence of metabolic syndrome (MS) all over the world, with rising trend among the younger population. Individuals with MS are at a higher risk of impaired cardiovascular autonomic function. **Aim and Objective:** Our study aims to understand the relationship between the MS and autonomic functions in order to improvise the wellbeing of the people who are at either risk of developing or are suffering from MS and promote healthy lifestyle. **Materials and Methods:** Heart rate variability (HRV) was recorded in 10 participants with MS. The HRV analysis included estimation of time domain parameters and frequency domain parameters, total power and low frequency/high frequency (LF/HF). **Results:** The HRV parameters showed a decrease in value along with a high LF/HF ratio in the study participants. **Conclusion:** The study shows that MS significantly leads to dysfunction of autonomic nervous system.

KEY WORDS: Metabolic Syndrome; Autonomic Function Tests; Heart Rate Variability

INTRODUCTION

Metabolic syndrome (MS) is increasingly becoming a worldwide epidemic at an alarming rate. MS targets all the age groups, with especially rising trend in the younger age group. It poses as a major risk factor for cardiovascular diseases (CVD) and other vascular events like stroke. The overall impact of infectious disease is showing a decreasing trend while the global burden of chronic diseases (e.g., CVD and diabetes) is on the rise. The incidence and prevalence of CVD are rapidly increasing in India and worldwide. According to estimation by the WHO, more than 300 million people worldwide will suffer from diabetes by year 2025.[1] By 2020, CVD will be the largest cause of disability and death in India.[2,3] The MS is an assemblage of risk factors for atherosclerotic CVD. The chief culprits responsible for the development of the major CVD have been suggested as insulin resistance along with adiposity.[4]

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The major features of the MS include central obesity, hypertriglyceridemia, low levels of high-density lipoprotein (HDL) cholesterol, hyperglycemia, and hypertension. MS is a threat not only to the population across the world but also is becoming a burden on public health policies and guidelines. The leading factors leading to MS are socioeconomic status, sedentary lifestyle, unhealthy nutritional habits, and stress. Therefore, exploration in MS provides an interdisciplinary forum to develop the pathogenesis and treatment of the cluster of conditions associated with MS. Obesity, endothelial dysfunction, insulin resistance, dyslipidemia, glucose intolerance, prothrombotic and pro-inflammatory states, hyperinsulinemia, hyperuricemia, hypertension, CVD, and polycystic ovarian syndrome are few of the long-term complications which tend to develop in MS if left untreated.[5]

The autonomic nervous system is responsible for the management of various crucial functions such as blood pressure, heart rate, thermoregulation, respiration, gastrointestinal, bladder, and sexual function. Autonomic dysfunction resulting in disturbance of autonomic pathways is a common finding in many diseases. Dysautonomia can pose a challenge in diagnosis and treatment as it consists of a wide spectrum of different disorders, which would require management of individual symptomatic complaints.[6]

Modern autonomic function tests (AFTs) are affordable, easy to perform, and most importantly non- invasive. These tests not only help in the determining the extent of involvement of ANS but also severity of autonomic failure. The high sensitivity of expand AFT helps even in the detection of subclinical autonomic system impairment. Assessment of AFT includes cardiovagal, adrenergic autonomic, and sudomotor functions testing.[7] These tests offer a detailed assessment of autonomic nervous system function required for further management of the condition.

The rising incidence of MS, especially in the younger generation, calls for an immediate interception to curb the rampant growth of the disorder as well as prevent the development of long-term complications. The diagnosis and monitoring the progress of disease is herculean task in the present day scenario. Limitations which include variations in measurement techniques, interviewer bias, and different definitions for risk factors and time periods of survey have been observed in studies published on the risk factors such as hypertension,[8] diabetes,[9] impaired fasting glucose, dyslipidemia,[10] overweight,[11] and obesity.[12]

Cardiac AFTs provide a simple and non-invasive method for the assessment of the sympathetic and parasympathetic control of cardiovascular system. The study of cardiac autonomic functions in MS can help in correlating between MS and cardiac complications and therefore help in early intervention and its prevention.

Our study aims to understand the relationship between the MS and autonomic functions in order to improvise the wellbeing of the people who are at either risk of developing or are suffering from MS and promote healthy lifestyle.

MATERIALS AND METHODS

The sample used in this study consisted of 10 subjects who had developed MS. All subjects were patients of Endocrinology Department, Ramaiah Medical College, Bengaluru.

Ethical clearance was obtained from the Ramaiah Medical College ethical committee for human research to conduct the study. Informed written consent was obtained from all the subjects for the study. Males and females of age group 18–50 years were taken as the study participants. The participants are one who fulfilled the criteria as described below (as per International Diabetes Federation 2006):[13] Central obesity defined as waist circumference with specific values for different ethnic groups [Table 1].

Moreover, any two of the four criteria as mentioned below:

- Triglyceride level: ≥150 mg/dl or specific medication
- HDL cholesterol: <40 mg/dl and <50 mg/dl for men and women, respectively, or specific medication
- Blood pressure: ≥130 mmHg systolic or ≥85 mmHg diastolic or specific medication
- Fasting plasma glucose level: ≥100 mg/dl or previously diagnosed diabetes mellitus or specific medication.

The patients with pregnancy, postpartum period, lactating, postmenopausal, undergone cardiac procedures such as stents and bypass surgery, serious medical illness (such as pulmonary, cardiac, hepatic, and renal), thyroid disorders, anemia, neoplasia, any infectious disease, on oral contraceptive pills and hormone replacement therapy, on β-blockers, amiodarone, lithium and steroid therapy, severe anxiety and major depression, smokers, and alcoholics were excluded from this study.

A brief history regarding diabetes, hypertension, and dyslipidemia was taken which included duration and medications. Subjects were advised not to take any beverages 2 h before investigation. General physical examination was done to assess the health status of the subjects. Blood pressure was recorded using sphygmomanometer. Waist circumference was measured to the nearest 0.1 cm at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest using a stretch resistant tape when standing with feet close together, arms at the side, and bodyweight evenly distributed.

About 5 ml of venous blood will be taken from all the subjects with due aseptic precautions in Vacutainer tubes and samples will be allowed to stand till they clot. After centrifugation and serum separation, the serum samples will be used to estimate the fasting glucose – hexokinase method, HDL – direct homogenous enzymatic colorimetric test, and triglyceride levels – glycerol phosphate oxidase enzymatic method.

After recording the biochemical and physical parameters, the tests for the assessment of heart rate variability (HRV) were performed. The instruments used were Rotronic Monitoring System (RMS) VAGUS hardware and RMS VAGUS software. For this, the heart rate was recorded in resting state (supine position) for 10 min after allowing the subject to rest for 5 min.

After the recording, HRV parameters were calculated using RMS VAGUS software. The parameters included time domain and frequency domain parameters. In time domain parameters, root mean square of successive differences (RMSSD) (ms)

and standard deviation of NN intervals (SDNN) (ms) were calculated. In frequency domain parameters, low frequency (LF) (ms^2), high frequency (HF) (ms^2), total power (TP) (ms^2), and LF/HF (ms^2) were calculated.

RESULTS

The mean age of cases was 34.7 ± 6.39 years. In time domain parameters, RMSSD and SDNN were estimated. RMSSD (ms) was 22.049 ± 15.67 and SDNN (ms) was 40.979 ± 31.25. In frequency domain parameters, total power, LF, HF, and LF/HF were estimated. The TP (ms^2) was seen to be 698.7 ± 184.25, LF (ms^2) was seen to be 27.45 ± 8.33, and HF (ms^2) was seen to be 20.34 ± 8.08. The LF/HF ratio was seen to be 1.51 ± 0.57 [Tables 2 and 3].

DISCUSSION

The results show a reduction in time and frequency domain parameters with sympathovagal imbalance.

The MS is increasingly becoming a major threat in all the age groups across the globe. Furthermore, each component of MS leads to increases risk of developing cardiac disorders and sudden cardiac death.[4,14-17] Cardiac AFT provides an easy and non-invasive measure to assess the involvement and damage to autonomic nervous system in an individual.[18] Studies have shown positive correlation between the cardiac autonomic dysfunction and MS.[19]

In our study, the HRV parameters were analyzed under the time domain and frequency domain parameters. For the assessment of time domain parameters, SDNN and RMSSD were calculated, and for the frequency domain parameters, LF, HF, and TP were evaluated. In our study, both SDNN and RMSSD showed a reduction in the MS group. In the frequency domain parameters, LF, HF, and TP also showed a reduction in the cases.

The LF/HF ratio demonstrated a higher value in the cases. The reduced HRV parameters and high LF/HF ratio suggest a sympathovagal imbalance with sympathetic predominance and decrease in HF marks a reduction the vagal activity.[18] The subjects in the study by Saito *et al.* demonstrated low RMSSD, low HF, and high LF/HF which were significantly associated with MS.[20] Ma *et al.* showed that the subjects with MS had significantly reduced SDNN, LF, and HF, but RMSSD showed no significant difference.[21]

Koskinen *et al.* showed that women with MS exhibit lower vagal activity along with sympathetic predominance and also that MS was associated with lower HF, LF, TP, and a high LF/HF.[22] The results of a study by Grassi *et al.* showed that MS leads to an increased sympathetic activation which, in turn, characterizes mild CHF.[23]

Table 1: Waist circumference according to ethnicity

Ethnicity	Waist circumference (cm)	
	Males	Females
Europeans, Sub-Saharan Africans, Middle-Eastern, and Eastern Mediterranean	≥94	≥80
South Asians Chinese, Ethnic South, and Central Americans Japanese	≥90	≥80

Table 2: Time domain parameters in the study participants

Subject	RMSSD (ms)	SDNN (ms)
1	20.86	31.31
2	50.04	49.86
3	23.79	124
4	9.13	15.94
5	5.2	16.77
6	9.98	35.32
7	43.82	37.85
8	7.12	19.66
9	25.7	41.53
10	22.85	37.55
Mean	22.049±15.67	40.979±31.25

Table 3: Frequency domain parameters in study participants

Subject	Total power (ms^2)	LF (ms^2)	HF (ms^2)	LF/HF
1	727	25.7	26.7	0.96
2	541	32.7	36.4	0.89
3	756	33	22.9	1.44
4	738	35	21.8	1.61
5	937	26.1	12.8	2.04
6	703	15	6.2	2.42
7	273	40.3	19.7	2.05
8	889	23.9	17	1.41
9	696	28.4	17.5	1.62
10	727	14.4	22.4	0.64
Mean	698.7±184.25	27.45±20.34	20.34±8.08	1.51±0.57

Thus, our study was found to be in accordance with most of the studies, wherein at least one of the HRV parameters is abnormal. The similarities in our study with the other studies can be attributed to the fact that affected subjects in all the studies fall in same age group.

There are evidences in support of theory which suggests implications of sympathetic innervation in pathogenesis of MS.[24,25] The homeostatic regulation of blood pressure, glucose, and insulin levels is basically dependent on the neuroadrenergic system.[26] The MS components, namely, visceral obesity, increased blood pressure, and insulin

resistance, have been observed to lead to an increased sympathetic drive.[27,28]

Development of obesity and increased risk of CVD in these individuals are a result of a complex interplay between the sympathetic nervous system and nutritional status of an individual.[29]

The future studies can focus on comparing the dysautonomia Indian population with other ethnicities so as to determine exclusive factors affecting Indian, which can thus help in developing improvised measures for the treatment and control. As seen in a study by Bathula *et al*., Indians on comparison with Europeans showed adverse cardiac autonomic function marked by decreased HRV which exposes them to higher risk of developing coronary heart disease,[30] which can be controlled with lifestyle and dietary adjustments.[31]

Limitations of the Study

There was no follow-up done to see the progression of dysautonomia with the lifestyle and nutritional modifications.

CONCLUSION

The results show decreased time and frequency domain parameters with a high LF/HF ratio which marks sympathovagal imbalance leaning toward sympathetic dominance.

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