RESEARCH ARTICLE

Assessment of heart rate variability among individuals with different risk levels for type 2 diabetes mellitus

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ABSTRACT

Background: Cardiac autonomic function is altered in type 2 diabetes mellitus (T2DM) individuals. It is evidenced by decreased heart rate variability (HRV). Decreased HRV results in cardiac autonomic neuropathy and increased risk for sudden cardiac death. Identifying individuals with high risk for T2DM can be an important approach to prevent or delay T2DM complications. In India, the Indian Diabetes Risk Score (IDRS) questionnaire was developed for screening Indian population. To the best of our knowledge, there are no data available evaluating HRV among adults with different risk levels for T2DM (categorized using IDRS).

Aim and Objective: In our study, we evaluated HRV among adults with different risk levels for T2DM. Materials and Methods: This study was done in the Department of Physiology, MAPIMS. It is a cross-sectional study done on 130 male and female staffs, attenders, and laboratory technicians working in MAPIMS. All the participants will be asked to complete the IRDS questionnaire. Then, based on the IRDS score, they are divided into Groups I, II, and III. In all the three groups, 5 min short-term HRV will be recorded using RMS Polyrite. Data were analyzed by SPSS 20.0 version software. One-way ANOVA was used to find any statistical difference between the groups. Correlations between the variables were done using Pearson correlation test. Results: Statistically significant ($P < 0.05$) difference in HRV between different risk levels for diabetes was determined by one-way ANOVA and the post hoc (Dunn’s) test revealed that HRV levels were significantly reduced in high risk, moderate risk when compared to mild risk group.

Conclusion: HRV levels reduced as the risk for diabetes increased, that is, HRV negatively correlated with the risk score.

KEY WORDS: Autonomic Dysfunction; Diabetic Risk Score; Heart Rate Variability; Indian Diabetes Risk Score Questionnaire; Type 2 Diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a non-communicable disease, which has increased worldwide in epidemic proportions, especially among old age, sedentary, and obese people. India ranks in the second in the world, with 19% of world’s total diabetic population.$^{[1,2]}$ Current reports say that in developing country like India, the younger adults are also been affected with T2DM.$^{[3]}$ Cardiovascular autonomic neuropathy (CAN) is a major complication of T2DM. CAN occurs, when the sympathetic and vagal nerves supplying the cardiovascular (CV) system are affected leading to disturbances in the heart rate (HR) and vascular dynamics.$^{[4]}$ Clinically, using the spectral analysis of HR variability (HRV), the action of sympathovagal nerves on sinoatrial node can be assessed in various disease conditions.$^{[5]}$ CAN is more common in type 2 diabetes patients with a prevalence of 34%. CAN noted even in individuals with pre-diabetes and metabolic syndrome due
to prolonged abnormal glucoregulation. Indian Diabetes Risk Score (IDRS) is a simple, cost-effective tool than oral glucose tolerance test for screening undiagnosed T2DM in India. IDRS uses four parameters such as individual’s age, gender, family history of diabetes, waist circumference (WC), and physical activity to assess individual’s risk for developing diabetes. In non-diabetic individuals, IDRS can be used in screening metabolic syndrome, identifying cardiometabolic risks, and arterial stiffness. In diabetic people, IDRS is associated with complications of diabetes such as neuropathy and peripheral vascular disease. The previous studies done on diabetes, associated reduced HRV with duration of disease, hyperinsulinemia, obesity, hypertension, and retinopathy and showed HRV as an independent risk factor for CV morbidity and mortality. Penčić-Popović et al. showed that the group classified as a slightly elevated risk for developing T2DM already had changes in time- and frequency-domain parameters of HRV when compared to the low-risk group. In their study, the Finnish Diabetes Risk Score (FINDRISC) was used to identify the individual’s risk for developing diabetes. To the best of our knowledge, there are no reports available assessing HRV among individuals with different risk levels for T2DM categorized based on IDRS.

MATERIALS AND METHODS

Study Design

The study was conducted in the Department of Physiology, MAPIMS, after obtaining approval from institute ethics committee from December 2019 to May 2020. It was a cross-sectional study, involved 270 male and female attendees who visited MAPIMS medical college and hospitals during the study period. The sample size was estimated assuming that 40% of people would have moderate- to high-risk scores. Sample size was estimated using the formula $n = \frac{Pq}{E^2}$, where prevalence ($P$) = 40%, ($q$) = 60%, relative error ($E$) = 15% of prevalence, and estimated sample size came out to be 266. In our study, we took a sample size of 270 participants.

Selection of Subjects

Subjects aged between 35 and 50 years working in MAPIMS Medical College and Hospitals were included in the study. They were divided into three groups based on IDRS score. GROUP I: Subjects with low risk (IDRS of <30); GROUP II: Subjects with moderate risk (IDRS of 30–50); GROUP III: Subjects with high risk (IDRS of >60). Subjects with diagnosed diabetes mellitus, hypertension, thyroid disorders, coronary disease, and other systemic illnesses (according to the medical history) were excluded from the study.

Experimental Design

In each study participant, diabetes risk was assessed using the IDRS questionnaire. Then, based on the IDRS score, they were divided into Groups I, II, and III. In all three groups, anthropometric parameters such as height (in cm) and weight (in kg) were recorded. Body mass index (BMI) was calculated using Quetelet’s index = Weight (kg)/(Height$^2$) (m). Then, 5 min short-term HRV was recorded using RMS Polyrite, as per Taskforce recommendations. First, the subjects were given 15 min of supine rest before starting the procedure to minimize anxiety. Stable basal supine blood pressure and HR were recorded by an oscillometric method using an automated blood pressure monitor. Following this, 5 min resting HRV was recorded by connecting lead II ECG. The acquired 5 min resting lead II ECG was carefully analyzed for ectopics and artifacts and meticulously removed manually. Using the R wave detector, the RR tachogram was extracted. From the RR tachogram, both frequency-domain and time-domain measures were computed using HRV analysis software (Kubios HRV, version 1.1 Finland). HRV parameters such as total power (TP), power in high-frequency range (HFnu), power in low-frequency range (LFnu), LF/HF ratio, and mean HR, square root of the mean squared differences of successive NN intervals (RMSSD), number of pairs of adjacent NN intervals differing by more than 50 ms (NN50), and percentage of NN50 (pNN50) were studied.

Statistical Analysis of Data

SPSS version 20 was used for statistical analysis. The demographic variables such as age, height, weight, BMI, and WC were expressed as mean with standard deviation. HR, blood pressure, and HRV parameters were expressed as mean with standard deviation and the intergroup differences were analyzed using one-way ANOVA test. “$P$” < 0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

The mean age and anthropometric indices such as height, weight, BMI, and WC of the study groups are given in Table 1.

HR and Blood Pressure Parameters

The mean HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), and mean arterial pressure (MAP) of the study groups are given in Table 2. Comparison of HR, SBP, DBP, PP, and MAP among the risk groups was done using one-way ANOVA and the Tukey post hoc test was performed to find the significant difference among the groups.

HRV Parameters

Comparison of HRV parameters among the risk groups was done using one-way ANOVA and the Tukey post hoc test was performed to find the significant difference among the groups. In HRV parameters, the TP and HFnu were significantly
less ($P < 0.005$) and LF/HF ratio was significantly high ($P < 0.005$) [Table 3] in high-risk group when compared to low-risk group. The time-domain indices of HRV such as mean HR and RMSSD were significantly decreased ($P < 0.005$) [Table 3] in high-risk group when compared to low-risk group.

**DISCUSSION**

In the present study, anthropometric parameters such as height, weight, BMI, and WC were assessed in all three groups. We found that none of these parameters showed statistical significance ($P < 0.005$) among the risk groups. The comparison of HR and blood pressure parameters among the risk groups is given in Table 2. There is no statistically significant ($P < 0.005$) difference in these parameters between the risk groups.

Table 1: Demographic characteristics of study participants ($n=270$)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.91±9.87</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.33±9.72</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>58.26±1.14</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>23.15±3.47</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>92.6±6.42</td>
</tr>
</tbody>
</table>

The values are expressed as mean (SD); BMI: Body mass index

Table 2: Comparison of basal heart rate and blood pressure among subjects in risk groups ($n=270$)

<table>
<thead>
<tr>
<th>Cardiovascular parameters</th>
<th>Total ($n=270$)</th>
<th>Low risk ($n=34$)</th>
<th>Moderate risk ($n=199$)</th>
<th>High risk ($n=37$)</th>
<th>$P$-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>77.7±9.9</td>
<td>74.2±3.73</td>
<td>76.68±4.45</td>
<td>80.93±4.30</td>
<td>0.910</td>
</tr>
<tr>
<td>SBP</td>
<td>119.35±12.3</td>
<td>116.26±3.42</td>
<td>118.83±5.49</td>
<td>120.57±6.05</td>
<td>0.501</td>
</tr>
<tr>
<td>DBP</td>
<td>76.9±12.4</td>
<td>72.67±4.86</td>
<td>75.3±7.12</td>
<td>78.08±4.90</td>
<td>0.904</td>
</tr>
<tr>
<td>PP</td>
<td>43.45±9.85</td>
<td>41.89±3.54</td>
<td>43.54±4.45</td>
<td>44.49±9.21</td>
<td>0.98</td>
</tr>
<tr>
<td>MAP</td>
<td>91.89±10.85</td>
<td>86.29±4.62</td>
<td>90.80±5.40</td>
<td>92.90±3.06</td>
<td>0.400</td>
</tr>
</tbody>
</table>

Values are expressed as mean (SD); comparison of variables between groups done using ANOVA. *$P<0.05$ is statistically significant, HR: Heart rate (bpm), SBP: Systolic blood pressure (mmHg), DBP: Diastolic blood pressure (mmHg), PP: Pulse pressure (mmHg), MAP: Mean arterial pressure (mmHg)

Table 3: Comparison of heart rate variability at rest among subjects in risk groups ($n=270$)

<table>
<thead>
<tr>
<th>HRV parameters</th>
<th>Total ($n=270$)</th>
<th>Low risk ($n=34$)</th>
<th>Moderate risk ($n=199$)</th>
<th>High risk ($n=37$)</th>
<th>$P$-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP</td>
<td>960.45±245.95</td>
<td>1367.94±141.9</td>
<td>978.31±123.9</td>
<td>632.56±98.53</td>
<td>0.002</td>
</tr>
<tr>
<td>LFnu</td>
<td>55.42±5.99</td>
<td>55.06±5.65</td>
<td>55.39±6.23</td>
<td>55.78±5.56</td>
<td>0.923</td>
</tr>
<tr>
<td>HFnu</td>
<td>43.85±4.67</td>
<td>50±3.85</td>
<td>43.79±3.66</td>
<td>39.96±3.64</td>
<td>0.001</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>1.97±0.68</td>
<td>0.86±0.34</td>
<td>1.88±0.45</td>
<td>2.89±0.32</td>
<td>0.000</td>
</tr>
<tr>
<td>Time domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean HR</td>
<td>79.32±7.59</td>
<td>67.28±4.07</td>
<td>78.56±3.7</td>
<td>89.70±4.14</td>
<td>0.003</td>
</tr>
<tr>
<td>RMSSD</td>
<td>17.14±7.68</td>
<td>30.83±3.94</td>
<td>17.01±4.76</td>
<td>8.63±2.041</td>
<td>0.001</td>
</tr>
<tr>
<td>NN50</td>
<td>30.18±11.66</td>
<td>31.50±12.38</td>
<td>30.34±11.9</td>
<td>28.78±10.38</td>
<td>0.730</td>
</tr>
<tr>
<td>pNN50</td>
<td>13.46±5.5</td>
<td>13.28±4.05</td>
<td>13.36±5.5</td>
<td>13.89±6.3</td>
<td>0.901</td>
</tr>
</tbody>
</table>

Values are expressed as mean (SD); comparison of variables between groups done using ANOVA. *$P<0.05$ is statistically significant, TP: Total power (ms²), LF: Low frequency (ms²), HF: High frequency (ms²), nu: Normalized units, Mean HR: Mean heart rate (bpm), RMSSD: Square root of the mean squared differences of successive NN intervals (ms); NN50: Number of pairs of adjacent NN intervals differing by more than 50 ms, pNN50: Percentage of NN50

We also evaluated HRV among individuals with different risk levels for T2DM, categorized based on the Indian Diabetic Risk Score.[7] HRV parameters such as LFnu, HFnu, TP, LF/HF ratio, RMSSD, mean HR, NN50, and pNN50 were assessed in all three groups. In the high-risk group subjects, the HRV parameters that measure cardiac vagal function such as TP, HFnu, and RMSSD were significantly decreased ($P < 0.005$) [Table 3], LF/HF ratio, an indicator of sympathovagal imbalance (SVI) and increased mean HR, a marker of cardiac sympathetic activity were significantly high ($P < 0.005$) when compared to the low-risk group subjects. However, LFnu, another marker of cardiac sympathetic activity, showed no significant difference between the groups.[11] These findings suggested that cardiac autonomic dysfunction by means of increased sympathetic and reduced parasympathetic activity exists in subjects with high-risk group for diabetes. Autonomic nervous system (ANS), through its sympathetic and vagal branches, controls organ systems, which are involved in energy mobilization. There should be a balance between these two ANS branches for the normal functioning of the body.[12] Increased LF/HF ratio and decreased TP, HFnu, and RMSSD in the high-risk group indicated an imbalance between these two systems with sympathetic hyperactivity and vagal withdrawal in the high-risk group. Increased sympathetic activation and reduced vagal tone for a long time in these individuals might result in abnormal glucoregulation which may progress from normoglycemia to pre-diabetes and diabetes state.
Study done by Penčić-Popović et al.,[12] showed that subjects with higher risk for Type 2 diabetes had impaired HRV in the form of decreased SDNN and reduced frequency domain parameters, without significant changes in sympathovagal balance (LF/HF ratio). However, in their study, the sample size was only 69 subjects and categorization of diabetic risk was done based on the FINDRISC. HRV parameters for this study were obtained from 24 h electrocardiogram Holter recordings. Another study done by Silva-E-Oliveira et al.,[13] showed that subjects with the highest FINDRISC had altered HRV suggestive of reduced parasympathetic and sympathetic activity. This study had less number of subjects in the high-risk group, which could have affected their results. Study done by Keerthi et al.,[14] found a significant association between SVI in terms of LF:HF ratio and IDRS in Indian adults with pre-diabetes and diabetes without any disease complications. In our study, we did not find any significant association between LF:HF ratio and IDRS. In their study, the subjects were grouped based on fasting blood glucose levels into prediabetes, newly diagnosed diabetes and control groups. The association between LF:HF ratio and IDRS was present only in the pre-diabetes and newly diagnosed diabetes group. In our study, the blood sugar levels of the study subjects were not measured and subjects were grouped based on IDRS.

Blood sugar levels such as fasting blood sugar, postprandial blood sugar, and HbA1C could have been assessed in each group and associated with HRV which was not possible due to money constraints. Further larger studies could be carried out to assess the risk for CV disease in subjects with higher risk for Type 2 diabetes.

CONCLUSION

From our study, it is evident that cardiac autonomic dysfunction by means of increased sympathetic and reduced parasympathetic activity occurs in the high-risk group for diabetes. The previous studies have associated cardiac CAN with old age, duration of diabetes, and also with comorbidities. The novelty of our study is we found altered HRV in subjects with high risk for diabetes when compared to subjects with low risk for diabetes. Studies done in the past decades have shown that impairment of HRV is closely associated with CV mortality and morbidity. Thus, early identification of impaired HRV could be the first sign of autonomic dysfunction in subjects with high risk for the development of Type 2 diabetes. With appropriate lifestyle modifications, both the reduced HRV and risk factors for diabetes, according to IDRS, can be reversed.

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REFERENCES


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