RELATIONSHIP BETWEEN PARENTAL HISTORY OF TYPE 2 DIABETES MELLITUS WITH THE SYMPATHOVAGAL BALANCE IN YOUNG ADULTS WITH COMPARABLE BMI, STRESS AND PHYSICAL ACTIVITY LEVELS

Shakthinag S¹, Sandip Sardesai²

¹PG student, ²Professor and Head, Department of Physiology, Goa Medical College, Goa, India

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Corresponding author: Sandip Sardesai

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Abstract

Background: With the heritability of Type 2 diabetes mellitus adding to the disease burden, it would be ideal to find screening tools to detect early changes that could be present in Euglycemic individuals with a genetic predisposition.

Objective: To study if the parental history of type 2 diabetes mellitus has an association with the time domain, frequency domain and nonlinear basal heart rate variability indices

Methods and material: This cross sectional study was conducted in the Physiology department of Goa Medical college over a period of 2 months on 70 Medical students between the age of 18-21 years, with low-moderate stress (PAS 10) and fair physical activity (PAI of American academy of health and fitness). Using an Inco Polyrite D instrument, data collection was done and the RR interval data was analysed using Kubios software for the basal Heart rate variability indices of time domain, frequency domain and nonlinear methods. Data was entered into Excel spreadsheet and analysed using SPSS version 14. Mann Whitney U test was done to test for statistical significance.

Result: The mean age of the sample was 18.94 ± 0.759 years and out of the 70 subjects who had participated in the study 36 (51.4%) subjects had a positive parental family history of type 2 diabetes mellitus while 34 (48.6%) subjects did not. Significant changes were observed in the LF (nu), HF (nu) and LF/HF ratio. A significantly higher LF.n.u (p value - 0.008) and LF/HF (p value- 0.008) was observed in group with family history and a significantly lower HF.n.u (p value - 0.007) was observed in the same group. No other significant changes were observed in time domain and non linear indices.

Conclusion: Frequency domain HRV may be useful as a predictive index for diabetes mellitus. The presence of higher sympathetic activity and lower parasympathetic activity in individuals (with comparable stress level, BMI, physical activity) having a positive parental history of diabetes mellitus might indicate an underlying autonomic imbalance

Keywords: Diabetes, Family history, Heart rate variability, HRV, parental history, Sympathovagal balance

Introduction

An increased risk of type 2 Diabetes mellitus has been studied in individuals whose parents have type 2 diabetes mellitus. Twin studies have confirmed the genetic attributability to the disease progress. Other known risk factors compounding to genetics include physical activity and body fat distribution.^{1,2}

HRV has emerged as a non-invasive tool in measuring the autonomic activity and represents the degree to which cardiac activity is modulated by the autonomic system to the changing environmental demands. Thus, it would be helpful to know if the measure of basal sympathovagal balance in young adults would be genetically influenced by presence of family history of Diabetes mellitus in parents.³

Materials and methods

A cross sectional study was conducted in the Physiology department of Goa Medical college over a period of 2 months (February 2018-March 2018).

70 Medical students between the age group of 18-21 years, who gave consent for the study, with low-moderate stress (as per perceived stress scale 10) and fair physical activity (as per Physical activity index of American academy of health and fitness) was included in the study. The study group consisted of 36 subjects who have a history of type 2 diabetes mellitus in parents and 34 subjects with no family history in parents.

Exclusion criteria- The subjects with high stress based on perceived stress scale 10 and those individuals with sedentary or very good, high grade of physical activity were excluded. Subjects with a family history of hypertension in parents, those with habit of alcohol intake or smoking and those treated with drugs that might affect the cardiac autonomic regulation were also excluded.

Data collection was done using INCO Polyrite D instrument. ECG limb leads were connected and the subject was made to lie supine. After giving a 10 min period of rest with spontaneous breathing, the baseline heart rate variability was measured for at least 5 min.

Data collection was carried out in the same room for all volunteers. Volunteers were instructed not to drink alcohol, caffeine or smoke for 24 h before evaluation. Data was collected between 2-5pm. The participant was in recumbent position, still and at rest, without talking during data collection.

The RR interval text files were later exported and analysed using Kubios HRV standard software (version 3.2.0)

Data was coded & entered into Microsoft excel sheet version 2019 and analyzed using SPSS software version 14 to see if it was normally distributed with Shapir wilks test. The kurtosis and skewness of the data was assessed. The histogram and QQ plot was visually analysed. The HRV variables were taken as dependant variables and the family history of type 2 diabetes mellitus as independent variable. It was seen that the data was not normally distributed and hence non parametric test was employed for the analysis. Mann Whitney U test was performed to test for statistical significance.

Ethical approval was taken from the Institutional Ethics Committee (IEC) of GMC before commencement of the study

Results

Table 1: Result of Mann Whitney U test done on time domain HRV indices between the two groups with and without a family history

Variable	Family History of Diabetes mellitus	N	Percentiles			Z	P value
			25 th	50 th (Median)	75 th		
MRR (ms)	Yes	36	696.8500	779.9000	889.4050	-1.034	0.301
	No	34	679.1600	754.5900	824.1050		
SDNN (ms)	Yes	36	27.03900	36.61000	44.56825	-1.199	0.231
	No	34	21.35325	33.30500	41.81500		
RMSSD (ms)	Yes	36	24.61750	36.90000	45.71500	-0.599	0.549
	No	34	26.38075	32.40500	43.40500		
NN50	Yes	36	26.00	76.00	106.00	-0.394	0.694
	No	34	24.50	53.50	102.25		
pNN50 (%)	Yes	36	5.83848	19.70500	28.73075	-0.717	0.473
	No	34	6.12190	12.54750	26.57150		
HRVT	Yes	36	6.50735	9.74145	12.47650	-0.511	0.609
	No	34	6.86765	9.19150	11.10275		
TINN (ms)	Yes	36	131.50	192.00	224.75	-0.917	0.359
	No	34	138.25	169.00	210.75		

p value <0.05 taken as significant

ms- millisecond, MRR- Mean RR interval, SDNN- Standard deviation of NN intervals, RMSSD- Root mean square of successive RR differences

NN50-Number of successive RR intervals that differ by more than 50 ms, pNN50- Percentage of successive RR intervals that differ by more than 50 ms,

HRVT- HRV triangular index, TINN- Triangular interpolation of NN intervals

The mean age of the sample was 18.94 ± 0.759 years and out of the 70 subjects who had participated in the study 36 (51.4%) subjects had a positive parental family history of type 2 diabetes mellitus and 34 (48.6%) subjects did not have a parental history of the disease (Figure 1)

Figure1: Distribution of subjects based on the family history of diabetes in parents

Table 2: Result of Mann Whitney U test done on frequency domain HRV indices between the two groups with and without a family history

Variable	Family History of Diabetes mellitus	N	Percentiles			Z	P value
			25 th	50 th (Median)	75 th		
LF (ms ²)	Yes	36	280.813	590.080	899.540	-1.398	0.162
	No	34	209.485	382.900	722.510		
HF (ms ²)	Yes	36	174.875	421.110	825.343	-.129	0.897
	No	34	237.983	476.345	707.213		
LF (nu)	Yes	36	48.4423	57.6045	69.7388	-2.673	0.008*
	No	34	39.0180	47.8050	56.9675		
HF (nu)	Yes	36	29.96175	42.36150	51.48075	-2.691	0.007*
	No	34	42.92250	51.55500	60.88250		
LH/HF	Yes	36	.9340	1.3550	2.3275	-2.674	0.008*
	No	34	.6360	.9200	1.3350		

*p value <0.05 taken as significant

ms- millisecond, LF- Low frequency, HF- High frequency, nu – normalized unit

Table 3: Result of Mann Whitney U test done on nonlinear HRV indices between the two groups with and without a family history

Variable	Family History of Diabetes mellitus	N	Percentiles			Z	P value
			25 th	50 th (Median)	75 th		
SD1 (ms)	Yes	36	17.40925	26.35000	35.00750	-0.764	0.445
	No	34	18.67525	22.91000	30.74200		
SD2 (ms)	Yes	36	31.85625	43.94000	54.27150	-0.658	0.510
	No	34	29.80525	41.52000	51.65225		
SD2/SD1	Yes	36	1.496075	1.692500	1.845000	-0.059	0.953
	No	34	1.440000	1.675700	1.918700		
ApEn	Yes	36	1.150000	1.201100	1.260375	-0.065	0.948
	No	34	1.147675	1.198000	1.276250		

p value <0.05 taken as significant

ms- millisecond, SD- standard deviation, ApEn- Approximate entropy

Table 1,2,3 shows the result of Mann Whitney U test on the HRV time domain, Frequency domain and Non linear indices respectively between the two groups (with and without family history of type 2 diabetes mellitus). No significant changes were seen in the time domain (table 1) and non linear indices (table 3) of basal heart rate variability.

In table 2, it can be seen that the median of LF(low frequency) was higher in the group with positive family history and the HF(High frequency) was higher in the group with no family history. But these were not significant changes (p value- 0.162, 0.897 respectively). However significant changes were observed in the low frequency (normalized unit), high frequency (normalized unit) and LF/HF ratio. A significantly higher LF.n.u(p value -0.008) and LF/HF(p value- 0.008) was observed in group with family history and a significantly lower HF.n.u(p value – 0.007)was observed in the same group.

Discussion

Positive family history of type 2 Diabetes mellitus results in an increased risk of type 2 diabetes mellitus and could be

endowed to both the genetic as well as the environmental factors that are shared among the family members.^{4,5}

According to our study, the group with a positive family history of type 2 Diabetes mellitus in parents showed significantly higher median of low frequency component (normalised unit) compared to the group with no family history. These subjects also had a significantly lower high frequency component (normalised unit)

The high frequency component is synonymous to the parasympathetic activity while the exact reason for low frequency component is still debatable in a short term recording. But both sympathetic and parasympathetic activity are said to play a role in it.^{3,6}

Thus LF/HF ratio would be a better indicator of the sympathovagal balance. In our study, there was a significant increase in the LF/HF ratio in the group with a positive family history of type 2 Diabetes mellitus have a higher sympathetic dominance over those individuals with no family history.

In a similar study by Satheeskumar⁷, the frequency component of 46 subjects aged 18-25 years with parental history of type 2 diabetes mellitus were compared with those of 50 volunteers no family history. Although LF/HF was higher in the group with family history, it was not statistically significant. The BMI and physical activity were comparable among the two groups as in our study, but the stress levels were not accounted for in that study.

In another study by Tamilselvan et al⁸, the frequency and time domain components were compared between study group with family history with control group and showed significant changes indicating a sympathetic dominance in individuals with family history. The study also evidenced a significantly lower parasympathetic activity in study group based on the time domain and frequency domain parameters. There was a significantly lower overall HRV (mean RR and SDNN) and lower parasympathetic activity(RMSSD,pNN50). However, such a result was not seen in our study. They did not however take into account the physical activity and the stress levels of individuals which could also be an independent risk factor.

Contributions of dyslipidaemia towards sympathovagal imbalance have been studied in subjects with family history of type 2 diabetes mellitus.⁹ Development of dysautonomia has also been attributed to insulin resistance.^{8,10} The role of leptin after being released from adipose tissue has also been highlighted.¹¹

But in a population of young individuals, with normal BMI, moderate levels of physical activity and comparable stress levels such as in our study shows that other factors could be partaking in disease progression. Fiorentini et al¹² has also shown that in populations with a predisposition, autonomic disturbances are present and are not necessarily dependant on insulin resistance.

Højbjørre et al¹³ studied the decreased capability to change between carbohydrate and fat based on change in substrate availability. It was also studied that during hyperinsulinemia, individuals having a family history of type 2 Diabetes mellitus were more likely to opt storage of glucose in adipose tissue.

A possible mechanism underlying our finding could be a low-grade inflammation. It has been suggested that autonomic imbalance could activate inflammation. Studies have explained the possibilities of a chronic inflammatory setting with increased sympathetic activity while the parasympathetic activity is required to restore the homeostasis after inflammation.^{14,15}

Limitations of study

No distinction was made between parenteral history of both parents and those with only one parents who have type 2 diabetes mellitus. The evaluation of blood lipid

profiles, the body fat mass index and other factors like food habits would have further helped us understand the cause for autonomic changes in healthy adults.

Conclusion

Frequency domain of basal heart rate variability measurement may be useful as a predictive index for diabetes mellitus. The presence of higher sympathetic activity and lower parasympathetic activity in individuals(with comparable stress level, BMI, physical activity)having a positive parental history of diabetes mellitus might indicate an underlying autonomic imbalance and is to be researched upon further.

Conflict of interest: None

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