Association of Rate Pressure Product and Cardiovascular risk in Type 2 Diabetes Mellitus.

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ABSTRACT:*The prevalence of Type 2 Diabetes Mellitus (T2DM) today at the Global level is 45 million and is assumed to become 642 million by 2050. T2DM is a major cause for cardiovascular complications and death. The heart rate and blood pressure are said to increase in response to increased myocardial metabolic demand. Rate Pressure product (RPP)is an easily measureable index of increased oxygen demand which can be used. The aimof the study was to find out the association between Rate pressure product and cardio vascular risk in Type 2 DM patients.The Study was conducted in Trichy SRM Medical College in the Department of Physiology and general Medicine in T2DM patients who came for regular checkup. A structured Proforma was used to collect sociodemographic details like age, gender and occupation, clinical history like duration of disease, exercise habits. General examination details, height, weight, BMI and HbA1c were measured. The Type 2 diabetes mellitus patients were categorized intotwo groups, Type 2 diabetes mellitus with cardiovascular Autonomic Neuropathy (CAN) and Type 2 diabetes mellitus without cardiovascular Autonomic Neuropathy (CAN). Resting blood pressure, heart rate was& ECG were recorded. Rate Pressure Product was measured for the patients with Type 2 Diabetes Mellitus which had a significant correlation with cardiovascular risk.(p<0.005)*
Key Words: *Cardiovascular Disease, Diabetes Mellitus, Rate Pressure Product.*

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I. Introduction

As of International Federation of Diabetes (IFD), worldwide 451 million people are suffering from diabetes, the prevalence will become 642 million by the year 2050[1]. More than 70% of patients with type 2 diabetes are at risk of cardiovascular disease[2].People with Type 2 diabetes mellitus (T2DM) are prone to develop complications like higher cardiovascular morbidity and mortality, than the non-diabetic subjects.[3]Pulse pressure has been used to predict cardiovascular risk in patients with Type 2 diabetes mellitus.[4]Rate Pressure Product which is an early measureable index is a reflector of myocardial oxygen demand and defines the response of coronary circulation to myocardial metabolic demands.[5]An increased Rate Pressure Product is an indicator of increase in myocardial metabolic demand which is met by increased coronary blood flow. Cardio vascular Autonomic Neuropathy is a serious and most common complication of Type 2 Diabetes Mellitus. TheRate Pressure Product is already high inType 2 diabetes mellitusand inCardiovascular Autonomic Neuropathy further increase in stress leads to increased cardiovascular risk as the body has little or no capacity to further increase myocardial perfusion.[6]The main aim of the study was to find out whether Rate pressure productcan be used topredict cardio vascular risk in Type 2diabetes mellitus, which is a non-invasive and cost effective method.

II. Aims and Objectives

- To find out the association between Rate pressure product and cardio vascular risk in Type 2 diabetes mellitus patients.

III. Materials and methods

This study was conducted with the informed consent of participants after obtaining Institutional Ethical Clearance approval, in a tertiary health care teaching Hospital, in the department of Physiology with the collaboration of department of General medicine. The subjectswere mostly farmers of lower socio economic status.
Study Design: Prospective observational Study.

Study Setting: Trichy SRM Medical College Hospital and Research Centre
Inclusion criteria: Known Type 2 diabetes mellitus patients who had regular check-up in the tertiary care Hospital, (both males and females n=400).
Exclusion criteria:

- Patients with Ischemic Heart Disease, Congestive heart failure and Cardiac arrhythmias.
- Patients on α blockers, β blockers, calcium channel blockers, diuretics, antiarrhythmic, and antipsychotics were excluded from study.

Period of study: Six months between January 2018 to June 2018
Data Collection and procedure:
A structured Proforma was used to collect sociodemographic details like age, gender and occupation, clinical history like duration of disease, exercise habits.General examination details, height, weight, BMI and HbA1c were measured. The Type 2 diabetes mellitus patients were categorized into two groups Type 2 diabetes mellitus with cardiovascular Autonomic Neuropathy(CAN) and Type 2 diabetes mellitus without cardiovascular Autonomic Neuropathy (CAN).Resting blood pressure and heart rate was recorded in all the subjects in supine position, at complete physical and mental rest. ECG was taken. Rate Pressure Product was measured. RPP = Systolic Pressure in mm Hg x Heart Rate in beats/min x 10-2.
Statistics: Statistical test was performed by SPSS software (for windows). Descriptive statistics, unpaired t- test, Person Correlation and ROC curve were used to analyze the data.

IV.   Results

Among the 400 Type 2 DM patientsthere was no statistically significant difference in Rate pressure product with regard to age. Males (112.12±16.61) have higher Rate Pressure Product than females (107.99±9.0) which was statistically significant($p<0.005$). There was a significant association between Lifestyle and Rate Pressure Product($p<0.005$).

While patients having HbA1c ≥ 7 mg/ dl had a higher Rate Pressure Product (119.93 ±14.19) than the patients with HbA1C <7 (97.65±12.56, $p<0.005$). A statistically significant difference ($p<0.005$) was found with lesser RPP (98.86±10.78) in patients with exercise habits and higher RPP (119.43±14.44) in patients without exercise habits. Duration of Type 2 diabetes mellitus is positively correlated with Rate Pressure Product indicating increased myocardial oxygen demand and cardiovascular complications. Diabetes of duration, ≥5 years shows significantly($p<0.005$) higher Rate pressure product (119.85 ± 14.45) than patients with lesser duration,< 5 years (100.58 ± 14.63).Type 2 diabetes mellitus patients with Cardio vascular Autonomic Neuropathy have shown statistically significant ($p<0.005$)increase in Rate Pressure Product(128.99 ± 5.45)than Type 2 diabetes mellitus patients without Cardio vascular Autonomic Neuropathy (110.38 ±17.38).Table 1.

Table1: Rate Pressure Product with regards to other variables:

Sl.no	Parameters		Heart rate/min	Systolic Blood pressure (mm Hg)	Rate Pressure Product X10-2 (mean)
1	HbA1c	<7 mg/dl n=236	75.70±6.9	128.62±6.3	119.93 ±14.19
		≥7mg/dl n=164	84.69±6.5	141.34±9.2	97.65±12.56
2	Exercise habits	YES n=168	76.3±7.04	129.06±7.5	98.86±10.78
		no n=232	84.3±7.13	141.24±8.9	119.43±14.44
3	Duration of Disease	<5 YEARS n=188	77.35±6.73	133.04±9.2	100.58 ± 14.63
		≥5 YEARS n=212	87.22±6.31	141.38±9.9	119.85 ±14.45
4	Cardio vascular Autonomic Neuropathy(CAN)	Type 2 DM with CAN n=9	92.8±1.7	138.89±6.3	128.99 ± 5.45
		Type 2 DM without CAN n=391	80.73±1.7	136.06±4.3	110.38 ±17.38

When Person Correlation was applied a statistically significant correlation was seen between, HbA1c (r=0.520, $p<0.005$)with Rate Pressure Product. While other parameters had no significant positive association with Rate Pressure Product. Figure 1
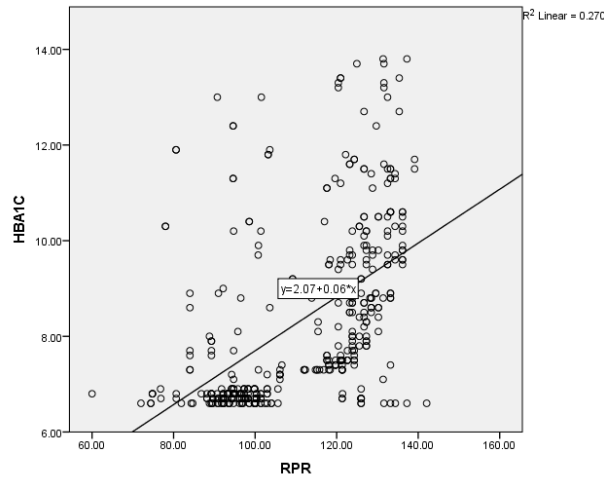
Figure 1: Correlation between Rate Pressure Product and HbA1c

ROC Curve: There is a overlap among parameters, so a ROC curve was plotted. An association between HbA1c and Rate Pressure Product was found. With area under curve was 84, with a sensitivity of 83% and specificity of 88%. The cut of value was found to be 112 x 10 [-2] for Rate Pressure Product, which was statistically significant(p<0.005) and is suggestive of cardiovascular risk. Figure 2, Table 2.
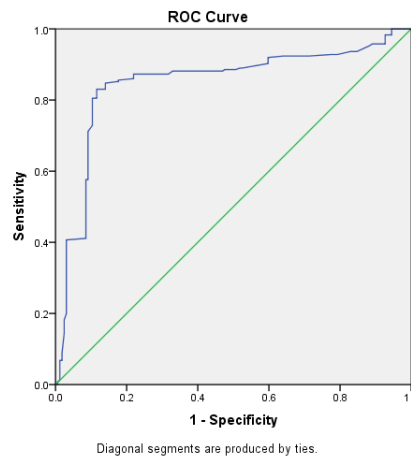

Figure 2: ROC Curve for Rate Pressure Product.

Table 2: ROC Curve Analysis for RPP:

Area Under Curve	Cut of value	Sensitivity	Specificity	Significance p value
84	112	83%	88%	<0.005*

V.   Discussion

India has become the Diabetic capital of the worldwith 6.5% of the youth affected with Type 2 Diabetes Mellitus[7]. Which predisposes the diabetic population to cardio vascular risk. Type 2 diabetes causes abnormalities in heart rate control in central and peripheral vascular dynamics.[5]Increased in both heart rate and systolic BP indicates increase in myocardial oxygen demand whichmay play a role in the development of silent myocardial ischemia.[8], This is represented by the non-invasive method rate-pressure product(RPP) which is the product of heart rate and systolic blood pressure.In previous studies, invasive methods were used to determine the oxygen consumption (VO2max) of an organ by collecting arterial and venous blood and subjecting it for blood gas analysis which is a tedious, time consuming process. A method which is more cost effective and easier to perform is required so that screening can be done and further medical intervention can be started to the earliest possible to prevent the adverse cardio vascular events[8].

In our Study there was a significant difference seen with regards to Gender with higher Rate Pressure Product in females when compare to males, which is in accordance to the study done byPremaSembulingam et.al.[9].A lesser Rate Pressure Product is an indicator of more parasympathetic nerve activity and parasympathetic tone which is believed to be cardio-protective. Accordingly, males seem to be safer with more

parasympathetically mediated cardio-protection than the females[9].Patients who had a sedentary Life style (118.16±14.81) and had no exercise habits showed a significantly greater rate pressure product than those who did heavy work(98.19±13.68) and had exercise habits. Sedentary life style is an a prelude to obesity which is further associated with insulin resistance and sympathetic over activity, increasing oxygen demand, increasing cardiac oxygen demandreflected by Rate Pressure Product as an indicator of cardio vascular risk[10].There was no significant difference with regards to age in our study.

Patients having higher HbA1c than ≥7 had higher Rate Pressure Product (119.93 ±14.19) when compared to patients with HbA1c<7 (97.65±12.56).Positive correlation was seen between Rate Pressure Product with HbA1c in our study. This was also seen in the study by Julie et al.[11] The increase in circulating glucose causes systemic vascular resistance, stiffness as the excess glucose binds to proteins, lipids, nucleic acids, resulting in the formation and accumulation of advanced glycation products in the vessel wall contributing to oxidative stress, inflammation and endothelial dysfunction causing increased rate pressure product and cardiovascular risk. [12-14]Duration of Type 2 DM has a significant association with Rate Pressure Product. The current study found out that lesser the duration (<5 years)lesser the RPP (100.58 ± 14.63).Higher the duration (≥ 5 years) higher theRate Pressure Product(119.85 ±14.45) in patients having Type 2 Diabetes Mellitus. Which is similar to the finding in the study bySegan et al.[15]Type 2 diabetes mellitus Patients with Cardiovascular Autonomic Neuropathy had higher RPP (128.99 ± 5.45) when compared with Type 2 diabetes mellitus patients without Cardiovascular Autonomic Neuropathy (110.38 ±17.38) which was also seen in the study bySegan et.al[15].Increasing duration of diabetes in patients causes the derangement of the autonomic system and thus causes cardiac autonomic neuropathy, the result of which there is increased Rate Pressure Productwhich in turn is due to sympathetic dysfunction. In addition to which the ventricular stiffness in DM and Hypertension, Hyperglycemia and Hyperlipidemia patients are vulnerable to various cardiac risk like silent Myocardial Infarction, Cardiac arrest and sudden death on exposure to stress[15].

VI. Conclusion

There is an association between rate pressure product and cardio vascular risk among Type 2 DM Patients. ThusRate pressure product can be used as a predictor for cardio vascular risk to prevent morbidity and mortality by early detection at a lower cost.

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