Gender Differences in Prediction of Cardiovascular Risk in Newly Diagnosed Type 2 Diabetics: A cross sectional study

Priyanka Banerjee [a*], Indira Maisnam[b], Jayanta Bhattacharya[a], Bulbul Mukhopadhyay[a]

[a]Department of Physiology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India.

[b]Department of Endocrinology, SSKM Hospital Kolkata, West Bengal, India.

Abstract

Background: Abdominal obesity is an independent determinant of cardiovascular risk in diabetics. Cardiac autonomic neuropathy is often not screened in newly diagnosed cases of diabetes. Early detection of sympathovagal imbalance recorded as decreased short-term heart rate variability of 5-minutes is a useful tool to detect cardiac autonomic neuropathy. Rate pressure product can measure myocardial oxygen consumption and cardiac sympathovagal activity.

Objectives: To find out the correlation between selected anthropometric parameters, gender and duration of diabetes with cardiac autonomic neuropathy in newly diagnosed type 2 diabetes mellitus patients.

Patients and methods: A cross-sectional study was conducted on 112 newly diagnosed type 2 diabetes mellitus patients of both genders at the Department of Physiology in collaboration with the Department of Endocrinology of R.G. Kar Medical College, Kolkata; West Bengal for one year.Body mass index was calculated using the Quetlet index. A ratio of (0.5) was considered a cut-off point for central obesity for waist height ratio for men and women. Short -term heart rate variability was measured in each study subject. Resting blood pressure and heart rate was recorded in all the subjects in supine position and rate pressure product was calculated.

Results:In the present study subjects rate pressure product was more in females (12.495±2.43) than males (10.955±1.62) which was statistically significant (p-value=0.0097). There was significantly more waist circumference and waist height ratio in patients in cardiovascular risk zone of rate pressure product of more than 10.00.Rate pressure product showed a positive association with duration of disease (r= +0.34) and p-value was significant.

Conclusion: We conclude that there is increased myocardial oxygen consumption and sympathetic drive evidenced by higher rate pressure product in women and in those with central obesity. Cardiac autonomic neuropathy might be present in newly diagnosed diabetes and longer duration of diabetes correlates with higher rate pressure product.

Keywords: Waist height ratio; Central obesity; Rate pressure product; Short term heart rate variability.

DOI: 10.21608/SVUIJM.2023.224501.1626

Correspondence: drpriyankabanerjee@gmail.com

Received: 28 July,2023.

Revised: 13 August, 2023.

Accepted: 21 August, 2023.

Published: 23 March, 2025

Cite this article as Priyanka Banerjee, Indira Maisnam, Jayanta Bhattacharya, Bulbul Mukhopadhyay. (2025). Gender Differences in Prediction of Cardiovascular Risk in Newly Diagnosed Type 2 Diabetics: A cross sectional study. *SVU-International Journal of Medical Sciences*. Vol.8, Issue 1, pp: 623-632.

Introduction

Diabetes mellitus (DM) can be broadly classified according to the pathogenesis process leading to hyperglycemia as type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and other specific forms of diabetes. Cardiac autonomic neuropathy (CAN) in T2DM is one of the major contributors to cardiovascular disease and death. The heart rate and blood pressure are increased in T2DM and obesity in response to increased myocardial metabolic demand and can be detected by rate pressure product (RPP). CAN is present in newly diagnosed T2DM patients without any prior history of ischemic heart disease and is associated with sudden death and increased mortality rate in patients **(Jyotsna et al., 2009).**

Newly diagnosed diabetes is taken as diagnosed within 2 years consistent with that of the American Diabetes Association **(American Diabetes Association, 2008)**. The increased prevalence of obesity is recognized as a major contributor to the rising prevalence of diabetes mellitus. The major cause of death in diabetes mellitus is cardiovascular disease. Abdominal obesity is an independent determinant of cardiovascular risk in diabetes and non-diabetes individuals. Waist circumference (WC) and waist-height ratio (WhtR), the indicators of abdominal obesity are predictors of cardiovascular health risk compared to other anthropometric measures, like the body mass index (BMI) **(Esteghamati et al., 2013)**. CAN in T2DM is associated with abnormalities in heart rate variability, decrease in baroreceptor sensitivity, and late manifestation of abnormal vascular dynamics **(Poanta et al., 2011)**. RPP, a product of heart rate and systolic blood pressure is used in our study as an accurate, noninvasive, and easily measurable index of myocardial oxygen consumption and an indirect measure of myocardial workload **(Jorgensen et al., 1977).**

It is found to be linked to a sympathovagal imbalance in obesity **(Indumathy et al., 2015)**. Lesser RPP indicates more parasympathetic tone which is cardio protective. Heart rate variability (HRV) gives information about the sympathetic-parasympathetic autonomic drives and alterations in HRV are observed much before the onset of clinical symptoms of cardiovascular disease. This highlights the role of HRV as an important and sensitive tool in the prediction of cardiovascular risks in patients with diabetes.

Early detection of the sympathovagal imbalance recorded as decreased short-term HRV of 5 minutes is a useful tool to detect CAN even within 2 years of diagnosis **(Balcıoğlu et al., 2015)**; and can predict cardiovascular disease and major cardiovascular events in obese T2DM **(Williams et al., 2019).**

The aim of the current study was to find out the correlation between selected anthropometric parameters namely BMI, abdominal obesity assessed by WhtR, WC; gender and duration of diabetes with cardiac autonomic neuropathy detected by an autonomic sympathovagal imbalance in newly diagnosed T2DM patients.

Patients and methods

The cross-sectional study was conducted on 112 newly diagnosed T2DM patients of both genders at the Department of Physiology in collaboration with the Department of Endocrinology of R.G. Kar Medical College, Kolkata, from September 2020 to August 2021. Ethical clearance was obtained from The Institutional Ethics Committee (20.1.2020, Registration No. ECR/322/ Inst/ WB/2013), of the R.G. Kar Medical College, prior to study.

Written consent was taken from the patients and confidentiality of their personal information was maintained.

Inclusion Criteria: Newly diagnosed T2DM (diagnosed within the last 2 years) of both genders, aged 30 years to 60 years, who consented to the study.

Exclusion criteria: Patients having symptoms of autonomic neuropathy, uncontrolled hyperthyroidism or hypothyroidism, known hypertensive, patients with underlying cardiovascular disease and any major systemic illness were excluded from the Study.

Data collection and procedure

A structured proforma was used to collect sociodemographic, clinical history and general examination details and fasting plasma glucose, postprandial plasma glucose were taken from history sheets of the subjects. Anthropometric parameters measured were weight (kg), height (cm), hip circumference (cm), waist circumference(cm), body mass index {BMI (kg/m2)} and waist-height ratio (WhtR).Height was measured at nearest 0.1cm without wearing a footwear by a stadiometer instrument. Weights of the subjects were measured in kilogram to the nearest 100 grams using a digital weighing machine. BMI was calculated using Quetlet index as per the formula weight in kilogram/ height in meter squared (**Garrow et al., 1985**).

Using a non-elastic tape, WC was measured at the mid-point between the lower costal margin and top of the iliac crest at the end of normal expiration,parallel to the floor.WhtR was calculated as WC (in cm) divided by height (in cm). A ratio of (0.5) was considered a cut-off point for central obesity for WhtR for men and women (**Yoo et al., 2016**). Central obesity has been defined in accordance with criteria specific for South-Asian populations with waist circumference in males > 90 cm and for females > 80 cm as cut-offs for central obesity (**Prasad et al., 2020**). The cut-offs for BMI in South Asians are: Normal BMI: 18.0-22.9 kg/m2, Overweight: 23.0-24.9 kg/m2, Obesity: >25 kg/m2 were considered (**Misra et al., 2009**).

Short-term HRV in each patient was measured and for that a 5-minutes of resting R-R intervals was recorded as per the standard procedures recommended by Task Force on HRV (Electrophysiology TF, 1996**).** Tea, coffee were not allowed within 12 hours prior to the HRV test.Patients were asked to report refraining from food at least for 2hrs.Patients were told not to take any sedative or any drug which might affect central nervous system before the test.Tight under-clothing wearing and metallic objects wearing were not allowed.The subjects were advised to have a sound sleep the night before recording HRV. Patients were encouraged to evacuate bladder before doing the test.Patients advised to avoid smoking in preceding 24hrs.The HRV recordings were taken in the morning in the neurophysiology laboratory of the physiology department maintaining optimal temperature and minimal light and standard guidelines were followed as far it was practicable.

The study tool used was Physiograph Polyrite-D instrument with bio-amplifiers, 4channels and accessories (RMS latest software-Version 3.0.16). A transducer mechanism was used for recording of short term HRV (5-minutes) and for that the limb electrodes (hand and foot electrodes) were connected to the bio-amplifier of the Polyrite-D machine. Frequency domain (spectral) and time domain analysis of short term (5min) HRV were recorded after 15 minutes of rest in lying down position. Time domain parameters of HRV analysis were taken like, Standard deviation of NN intervals (SDNN), root mean square of successive differences (RMSSD). Standard deviation (SD) of RR or NN intervals SDNN represents day-night variability in heart rate and was given more emphasis for long term heart rate variability. RMSSD is the primary time domain parameter which can estimate the vagally mediated changes in HRV.The HF component of HRV indicates the cardiac vagal drive to the heart which represents parasympathetic activity. The Low frequency component of

HRV, is not a sole representative of cardiac sympathetic drive, but also has parasympathetic components. The sympathovagal balance is assessed by the LF-HF ratio. LF-HF ratio in normal population may vary from 0.5 to 1.5.A continuous short term electrocardiogram (ECG) recording was done.

Time domain analysis signified the change in the resting heart rate overtime, whereas Frequency domain (power spectral density) recorded frequency and amplitude of different periodic oscillations of the heart rate. The normal sinus rhythm intervals (NN) were obtained after removing the artifacts. The protocols used are different from each other for various studies and we get more than one HRV numbers. So to analyse the in-depth reliability of short term HRV test, the most commonly used HRV parameters were considered for relative as well as for absolute reliability. We followed the guidelines of The task force which was constituted by the European Society of Cardiology and North American Society of Pacing, to develop appropriate terminologies with its definitions, protocols and standards of HRV measurements **(Shaffer F et al., 2017).** Also considering as general rule we have taken normal range of HRV values according to upper and lower 95% confidence limit in this study. The resting heart rate was documented from the Physiograph Polyrite–D instrument.Resting blood pressure was recorded in all the subjects in supine position, at complete physical and mental rest. Rate pressure product (RPP) was measured as follows:

RPP = Systolic blood Pressure (mm Hg) x Heart Rate (beats/min).

Statistical analysis

After collection of data, all the data were tabulated in MS-EXCEL sheet.The statistical tests were performed using the Statistical Package for Social Sciences SPSS software (IBM, SPSS) version 23.0. The tests used were Unpaired t-test, Pearson correlation study and scatter diagram for data analysis in the present study .The results where p-value was <0.05, were considered as statistically significant results.

Results

Result shows (**Table.1**) that mean BMI(kg/m^2) was more in females (28.16±3.08) than males (26.26±1.57) which was statistically significant (p=0.0082). Mean waist circumference (cm) in females (93.44±4.82) was more than males (91.04±7.90) but was statistically not significant (p=0.1659). Mean height (cm) was more in males (162.88 ±4.64) than females (153.88±5.89) with the difference statistically very significant (p =0.0001). Waist-height ratio was significantly high in females (0.61+/-0.03) than males (0.56+/-0.05) (p-value 0.0001). There were no statistically significant differences in duration of diabetes mellitus, fasting plasma glucose (p-value=0.099), post-prandial plasma glucose (p-value=0.69) between males and females.

Table.1 Baseline characteristics of the study subjects

Variables	Male Mean±SD	Female Mean±SD	p-value
Body mass index(kg/m2)	26.26 ± 1.57	28.16 ± 3.08	0.0082*
Waist circumference(cm)	91.04 ± 7.90	93.44 ± 4.82	0.1659
Height(cm)	162.88± 4.64	153.88± 5.89	0.0001*
waist height ratio	0.56± 0.05	0.61± 0.03	0.0001*
Duration of DM(month)	14.54 ± 5.69	14.59 ± 5.86	0.97
Fasting plasma	137.38± 31.69	160.47 ± 61.49	0.099

glucose(mg/dl)			
Postprandial plasma glucose(mg/dl)	228.63± 78.26	238.38± 100.24	0.69

*p-value <0.05 was considered statistically significant

(**Table.2**) shows RPP was more in females (12.495±2.43) than males (10.955±1.62) which was statistically significant (p-value=0.0097).HRV analysis showed More SDNN value in male (45.21±28.94 ms) than female (43.42±46.47ms), but the difference was not statistically significant (p-value=0.8692). There was no statistically significant difference of the root mean square of the successive differences (RMSSD) in milliseconds (ms) between male (40.88±37.90) and female (43.51 ±57.91) (p- value= 0.8923).The frequency domain LF:HF ratio was more in female (1.5±0.9) than male (0.99±0.6),and it was statistically very significant(P= <0.05).

Table.2. Comparison of cardiovascular risks among female and male

CV RISKS	Female	Male	p-value
RPP(mm Hg × beats/min)	12.495±2.43	10.955±1.62	0.0097*
SDNN(ms)	43.42 ± 46.47	45.21 ± 28.94	0.8692
RMSSD(ms)	43.51 ±57.91	40.88±37.90	0.8923
LF:HF	1.5±0.9	0.99±0.6	0.0009*

*p-value <0.05 was considered statistically significant

The subjects were categorized in normal zone and cardiovascular risk zone according to their RPP. RPP more than 10.00 was taken as indicator of increased cardiovascular risk in those subjects. (**Table.3**) shows there was significantly more WC and WhtR in patients in CV risk zone of RPP of more than 10.00.

Table.3. Distribution of waist circumference and waist height ratio in different risk zones of RPP

RPP(mm Hg × beats/min)	Waist circumference(cm) Mean±SD	Waist height ratio Mean±SD
Normal zone	88.69±8.78	0.55± 0.06
Risk Zone	93.53±5.06	0.60± 0.04
P- value	0.0149*	0.0035*

*p-value <0.05 was considered statistically significant

Pearson correlation study was done (**Table.4**) and we found that RPP had a positive association with BMI (kg/m^2) and it was statistically very significant (p=0.004). Waist height ratio (r=+0.47) (**Fig.1**) and waist circumference (r-value=+0.328), both the correlations with RPP were also statistically significant (p<0.05). RPP showed a positive association with duration of disease (r= +0.34) (**Fig.2**), and it was statistically significant p-value (0.01).The time domain parameter of HRV Standard deviation of NN interval (SDNN)(ms) had negative association (r=-0.1918) with RPP, but the result was statistically non-significant (p-value=>0.05).The frequency domain parameter of HRV LF:HF ratio(a ratio of low frequency to high frequency) had positive correlation with RPP(r=+0.049),but the result was non-significant(p-value=0.72).

Table.4. Pearson correlation of waist height ratio, waist circumference, duration of disease, SDNN and LF:HF ratio with RPP

Variables	RPP(mm Hg × beats/min)	
	r -value	P- value
Body mass index(kg/m²)	+0.38	0.004*
Waist height ratio	+0.47	0.003*
Waist circumference(cm)	+0.328	0.013*
Duration of diabetes mellitus (month)	+0.34	0.01*
SDNN(ms) Standard deviation of NN	-0.1918	0.156
Low frequency :high frequency(LF:HF) ratio	+0.049	0.72

*p-value <0.05 was considered statistically significant

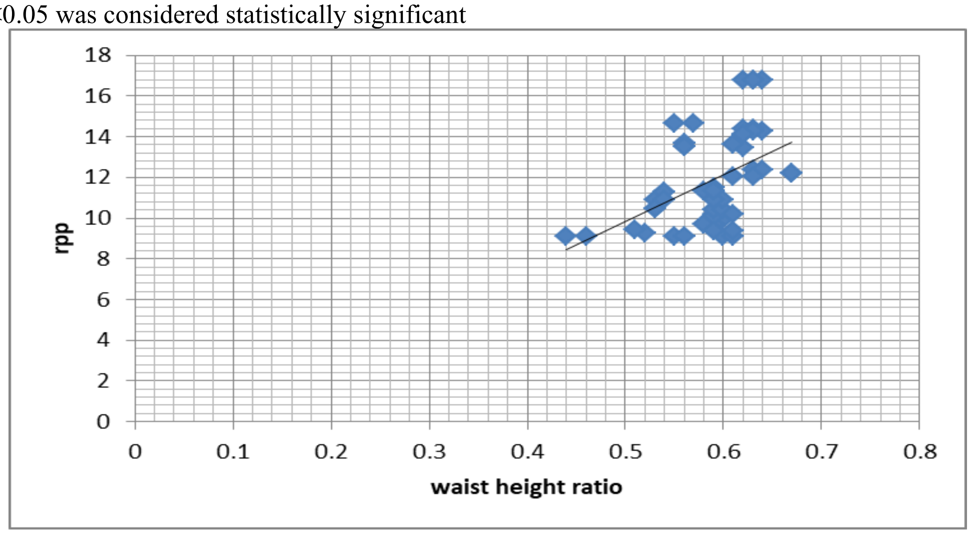

Fig.1. Correlation of waist height ratio with rate pressure product (RPP)

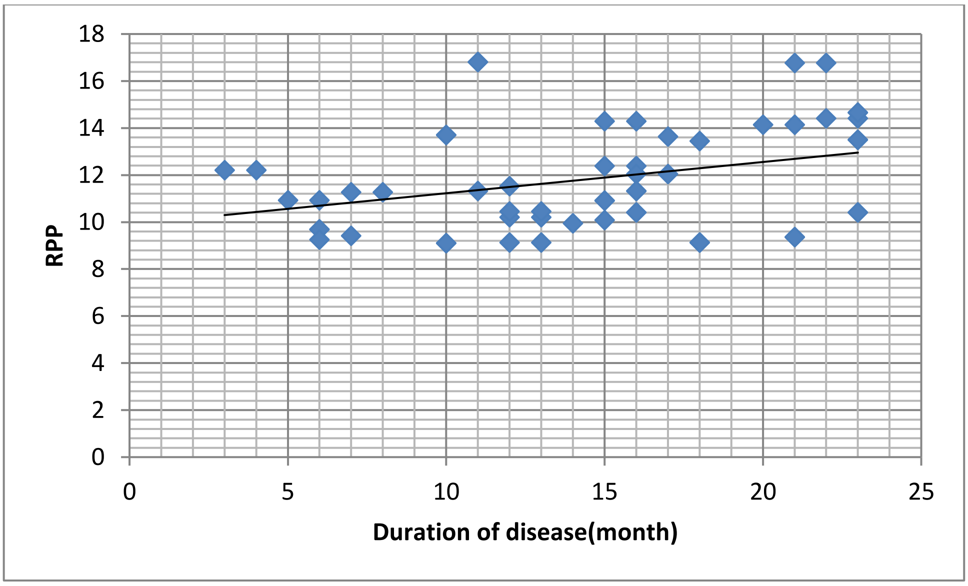

Fig.2. Correlation of duration of disease with rate pressure product (RPP)

Discussion

Ewing et al. (1970) proposed some simple autonomic functions tests as a predictor of CAN. Further studies attested that study of HRV can be used in diagnosing CAN even at subclinical stage of the disease, can detect sympatho-vagal imbalance and thus provides us the possibility of better prediction and prevention in progression of diabetic CAN and metabolic syndrome **(Balcıoğlu et al., 2015)**.

In the study subjects mean of WC and WhtR both were more in females than males. Central adipose tissue, is now considered as an 'early health risk' and WhtR is widely used to measure it. WC is a good indicator of abdominal obesity and a better predictor of cardiovascular risk than BMI. So in the present study subjects females can be predicted to be more prone to CV risk than males due to their more abdominal obesity.

In the present study it was seen that there was a significant difference in higher RPP in females compared to males. This is different from previous study done by **Sembulingam et al. (2015).** The earlier study of **Sembulingam et al. (2015)** found RPP to be increased significantly in males and non-significantly in females after physical stress.

In a previous study by **Jena et al. (2017)** it was found that abdominal obesity, hemodynamic variable like RPP were increased due to increase in sympathetic tone. This is similar findings of the present study.

Russo et al. (2021) in study found that obesity is associated with insulin resistance and the resultant hyperinsulinemia is associated with sympathetic overactivity in T2DM which gives may explain the increase in parameters of hemodynamic variables in present study subjects. **Scherrer et al. (1997)** in a study had similar findings.

Cardiovascular diseases develop on an average 10 years later in women compared to men. One of the major reasons for this cardiovascular protection is endogenous estrogen in pre-menopausal women. Menopause is associated with estrogen insufficiency and is associated with the loss of cardiovascular protection which pre-menopausal women have over men.

Evangelista et al. (2009) found in their study that women with diabetes were not well-controlled and were more prone to die from cardiovascular events.

Increased RPP has been reported as an established risk of CVD **(White, 1999)**. A lesser RPP is an indicator of more parasympathetic nerve activity and parasympathetic tone which is believed to be cardio-protective. Accordingly, in our study males seem to be more cardiovascular protected with more parasympathetically mediated cardio-protection than the females.

HRV study showed more SDNN in males than females which was not statistically significant. Lower SDNN value indicated more sympathetic drive in female patients in compare to males.

Few studies suggest that in general, the incidence of a new myocardial infarction is higher in men than in women **(Booth et al., 2006)**. The development of diabetes, caused women to lose the cardiovascular protection they have compared to men, still unforeseen CV events are still higher in men **(Huxley et al., 2006)**.

In the present study RMSSD (ms) (time domain parameter of HRV) which is an indicator of parasympathetic drive is slightly more in females, but result was not statistically significant. Helleputte S et al., found in a study that HRV measures (RMSSD) could be used as predictors of glycemic control in patients with diabetes **(Helleputte et al., 2020)**. In our study females were more hyperglycemic than males, though the findings were not statistically significant.

Our study result showed high LF/HF ratio in females in compared to males,which indicates sympathovagal imbalance was more in women. **Mirza et**

al. (2012) found more damage of parasympathetic nerve in DM and they told that axonal degeneration of long parasympathetic nerves like vagus is mostly caused due to chronic uncontrolled diabetes.In our subjects female patients had more fasting and postprandial plasma glucose than males. Obesity solely can also impair cardiac autonomic function in type 2 diabetics **(Valensi et al., 2003)**.

The subjects were distributed in normal zone and cardiovascular risk zone according to their RPP. There was significantly more WC and WhtR , the markers of abdominal obesity, in patients in CV risk zone of RPP of more than 10.00,whereas under resting conditions, safer RPP is considered in the range of 7.00 and 9.00 (**Fletcher et al., 1979**). It may imply that abdominal obesity results in more CAN risk.

Pearson correlation study showed significant positive association of RPP with BMI, WC (cm) and WhtR. WhtR had a moderate positive association with RPP and it was very significant(p=0.003). The results showed that in those subjects higher central obesity was associated with more myocardial oxygen demand and sympathetic drive.The BMI had a weak positive correlation with RPP. Central (intra-abdominal) distribution of fat are much more extensively linked to insulin resistance, type 2 diabetes, and cardiovascular complaint than are peripheral (gluteal/subcutaneous) fat depots. Visceral fat is more inflammatory and lipolytic which can cause insulin resistance. Also lesser capacity to hold fat in the subcutaneous sites may result in fat overflowing to visceral and ectopic sites.

Duration of DM had a moderate positive association with RPP (r=+0.34,p=0.01) . Even within 2 years of diagnosis of T2DM, patients presented with sympatho-vagal overdrive, which is as an indicator of CAN in a very early stage of the disease. In the present study the longer duration of Type 2 DM among newly diagnosed cases had a significant association with RPP, which is analogous to the finding in the study by **Segan et al. (2011**).

SDNN showed weak negative association with RPP,SDNN value over 100 milliseconds (ms) can be considered normal, SDNN value less than 50 ms is considered high-risk, and a SDNN between 50-100 ms can indicate moderate risk, they are related to cardiovascular risks **(Corrales et al., 2012)**.

RPP showed positive correlation with LF:HF ratio, indicating that the myocardial work load increases with increase in Sympathovagal imbalance.

Limitations: It was a cross sectional study so the causal relationship could not be assessed. Short term HRV analysis is a 5 minutes snapshot of long-term study of 24 hours duration.

Future prospective: In future research with different study designs and metacentric approach may enrich our findings.A gender-oriented approach can be taken in respect to assess and prevent different CV risks in diabetic patients. In women patients, pre and postmenopausal age group may be considered in future. Grouping of subjects according to their HBA1C can be taken into account.

Conclusion

The present study showed the presence of CAN indeed in newly diagnosed T2DM. Longer duration of diabetes correlated with higher RPP.In Overall study subjects central obesity was associated with presence of higher RPP.Females had greater sympathetic overdrive than males in those study subjects. Central obesity could be an important cause of this potential threat to women even before postmenopausal age of estrogen deficiency.

We conclude that CAN can be present in newly diagnosed T2DM and that there is increased myocardial oxygen consumption evidenced by higher RPP in women and in those with central obesity. We therefore suggest that early assessment of cardiac autonomic function is necessary so that it can be managed appropriately in a timely fashion.

Conflict of interest: None.
Source of funding: None.

References

- **American Diabetes Association. (2008).** Diagnosis and classification of diabetes mellitus. Diabetes care, 31 Suppl 1: S55–S60.
- **Balcıoğlu AS, Müderrisoğlu H. (2015).** Diabetes and cardiac autonomic neuropathy: Clinical manifestations, cardiovascular consequences, diagnosis and treatment. World journal of diabetes, 6(1): 80–91.
- **Booth GL, Kapral MK, Fung K, Tu JV. (2006).** Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. Lancet (London, England), 368(9529): 29–36.
- **Corrales MM, Torres BDE, Esquivel AG, Salazar MA, Naranjo OJ. (2012).** Normal values of heart rate variability at rest in a young, healthy and active Mexican population. Health, 04(07): 377–385.
- **Esteghamati A, Mousavizadeh M, Noshad S, Shoar S, Khalilzadeh O, Nakhjavani M. (2013).** Accuracy of anthropometric parameters in identification of high-risk patients predicted with cardiovascular risk models. The American journal of the medical sciences, 346(1): 26–31.
- **Electrophysiology, T. F. (1996).** Heart rate variability. Circulation, 93(5): 1043–1065.
- **Ewing DJ, Campbell IW, Clarke BF. (1980).** Assessment of cardiovascular effects in diabetic autonomic neuropathy and prognostic implications. Annals of internal medicine, 92: 308–311.
- **Evangelista O, McLaughlin MA. (2009).** Review of cardiovascular risk factors in women. Gender medicine, 6 Suppl 1:17–36.
- **Fletcher GF, Cantwell JD, Watt EW. (1979).** Oxygen consumption and hemodynamic response of exercises used in training of patients with recent myocardial infarction. Circulation, 60(1): 140–144.
- **Garrow JS, Webster J. (1985).** Quetelet's index (W/H2) as a measure of fatness. International journal of obesity, 9(2): 147–153.
- **Huxley R, Barzi F, Woodward M. (2006).** Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies. BMJ (Clinical research ed.), 332(7533): 73–78.
- **Helleputte S, De Backer T, Lapauw B, Shadid S, Celie B, Van Eetvelde B, et al. (2020).** The relationship between glycaemic variability and cardiovascular autonomic dysfunction in patients with type 1 diabetes: A systematic review. Diabetes/metabolism research and reviews, 36(5).
- **Indumathy J, Pal G K, Pal P, Ananthanarayanan P H, Parija SC, Balachander J, et al. (2015).** Association of sympathovagal imbalance with obesity indices, and abnormal metabolic biomarkers and cardiovascular parameters. Obesity research & clinical practice, 9(1): 55–66.
- **Jyotsna VP, Sahoo A, Sreenivas V, Deepak K. (2009).** Prevalence and pattern of cardiac autonomic dysfunction in newly detected type 2 diabetes mellitus. Diabetes Research and Clinical Practice, 83(1): 83–88.
- **Jorgensen CR, Gobel FL, Taylor HL, Wang Y. (1977).** Myocardial blood flow and oxygen consumption during exercise. Annals of the New York Academy of Sciences, 301: 213–223.
- **Jena S, Purohit K, Mohanty B. (2017).** Correlation of anthropometric indices with rate pressure product in healthy young adults. Muller Journal of Medical Sciences and Research, 8(2): 82.
- **Misra A, Chowbey P, Makkar BM, Vikram N K, Wasir JS, Chadha D, et al. (2009).** Consensus statement for

diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. The Journal of the Association of Physicians of India, 57: 163–170.

- **Mirza M, ANR L. (2012).** A comparative study of heart rate variability in diabetic subjects and normal subjects. International Journal of Biomedical and Advance Research, 3(8):640-4.
- **Poanta L, Porojan M, Dumitrascu DL. (2011).** Heart rate variability and diastolic dysfunction in patients with type 2 diabetes mellitus. Acta diabetologica, 48(3): 191–196.
- **Prasad DS, Kabir Z, Revathi DK , Peter PS, Das BC. (2020).** Gender differences in central obesity: Implications for cardiometabolic health in South Asians. Indian heart journal, 72(3): 202–204.
- **Russo B, Menduni M, Borboni P, Picconi F, Frontoni S. (2021).** Autonomic Nervous System in Obesity and Insulin-Resistance-The Complex Interplay between Leptin and Central Nervous System. International journal of molecular sciences, 22(10): 5187.
- **Shaffer F, Ginsberg JP. (2017).** An Overview of Heart Rate Variability Metrics and Norms. Frontiers in Public Health, 5.
- **Sembulingam P, Sembulingam K, Ilango Saraswathi, G Sridevi. (2015).**Rate Pressure Product as a Determinant of Physical Fitness in Normal Young Adults, IOSR Journal of Dental and Medical Sciences, 14(4): 08-12.
- **Scherrer U, Sartori C. (1997).** Insulin as a vascular and sympathoexcitatory hormone: implications for blood pressure regulation, insulin sensitivity, and cardiovascular morbidity. Circulation, 96(11): 4104–4113.
- **Segan DR. (2011).** Rate pressure product in type 2 diabetic cardiac autonomic neuropathy. Indian Journal of Applied Research, 1(11): 108–109.
- **Valensi P, Pariès J, Attali J. (2003).** Cardiac autonomic neuropathy in diabetic patients: influence of diabetes duration, obesity, and microangiopathic complications—the french multicenter study. Metabolism, 52(7): 815–820.
- **Williams SM, Eleftheriadou A, Alam U, Cuthbertson DJ, Wilding JPH. (2019).** Cardiac Autonomic Neuropathy in Obesity, the Metabolic Syndrome and Prediabetes: A Narrative Review. Diabetes therapy: research, treatment and education of diabetes and related disorders, 10(6): 1995–2021.
- **White WB. (1999).** Heart rate and the rate-pressure product as determinants of cardiovascular risk in patients with hypertension. American journal of hypertension, 12:50S–55S.
- **Yoo EG. (2016).** Waist-to-height ratio as a screening tool for obesity and cardiometabolic risk. Korean journal of pediatrics, 59(11): 425–431.