

Variation in Autonomic Function (Cans) Tests in Young Adults with and Without Parental History of Diabetes Mellitus

Ankita Grover, Richa Rai, Priyanka Chugh

Abstract— Introduction: Many studies have shown that children of diabetic parents are more likely to develop Diabetes, but very few studies have been done to find out early variation in autonomic function tests as an effect of Diabetes in normal children of diabetic parents.

Aim & Objective: To assess and study any variation in autonomic function (CANS) tests among normal young adults, within the age group of 18-25 years, with and without parental history of Diabetes Mellitus.

Method: Incidental sampling was done and 66 normal young adults were divided into two groups-CNDP (children of non-diabetic parents) and CDP (children of diabetic parents). Each subject underwent autonomic function (CANS) tests and their readings were noted.

Results: Difference between means of CNDP and CDP groups was compared by t-test. No significant difference was found in Expiration-Inspiration Difference (E-I), Valsalva Ratio (VR) and Change in Diastolic Blood Pressure (Δ DBP) in CDP group when compared to CNDP group.

Conclusion: There is no significant variation in autonomic function (CANS) tests among normal young adults with and without parental hi of Diabetes Mellitus.

Index Terms— Diabetes Mellitus, Expiration Inspiration Difference (E-I), Sustained Hand Grip, Valsalva Ratio (VR)..

I. INTRODUCTION

Our cardiovascular system is governed by autonomic nervous system¹. Diabetes mellitus is a group of metabolic diseases characterized by hyper-glycemia resulting from defects in insulin secretion, insulin action, or both². **One of the most overlooked of all serious complications of diabetes is cardiovascular autonomic neuropathy (CAN), which encompasses damage to the autonomic nerve fibers that innervate the heart and blood vessels resulting in abnormalities in heart rate control and vascular dynamics³.** Many studies have been shown that children of diabetic patients are more likely to develop Diabetes, but very few studies have been done to find out early variation in autonomic function tests as an effect of Diabetes in normal children of diabetic parents. This study was directed to assess and study any variation in autonomic function tests among normal young adults with and without

parental history of Diabetes Mellitus before clinical symptoms become overt in normal (non diabetic) children with parental history of Diabetes Mellitus.

II. METHODOLOGY

In this Cross sectional and observational study of subjects of age group 18 to 25 years^{4, 5}, normal BMI (18.5-24.9 kg/m²)^{6, 7}, sedentary⁸, non-smokers^{9, 10}, non alcoholic¹¹ individual who understand written and verbal English language and consented to participate were included.

Subjects with Parental h/o any medical/systemic condition (apart from T2DM) which may affect outcome of the study; subjects with any history of/diagnosed case of: diabetes, acute or chronic respiratory disorder, cardio-vascular disorder, neurophysiologic disorder, neuro-psychiatric disorder or any other illness known to effect the functioning of the autonomic nervous system, musculoskeletal disorder, established disease of other major organs, pregnancy trauma or surgery which may affect outcome of the study; on any regular medication or who answered "YES to one or more questions" on PAR-Q were excluded. The Outcome Measures of the study were Expiration Inspiration Difference (E-I) in terms of heart rate, Valsalva Ratio (VR) and Sustained Hand Grip in terms of Δ DBP (mmHg).

Procedure-66 subjects were subjected to the autonomic function tests as per the protocol. All the tests were performed using CANS504 analyser^{12, 13}. Baseline value of HR and BP and running ECG was taken by the software before performing autonomic function tests. The tests that were used in our standard cardiovascular autonomic function assessment are: Heart rate responses to the Valsalva manoeuvre⁴, Heart rate responses to deep breathing (maximum-minimum heart rate)⁴ and Blood pressure responses to sustained handgrip⁴. These parameters were thus compared statistically by dividing data into two groups.

III. RESULTS

Continuous data were summarized as Mean \pm SD while discrete data (categorical) in numbers and percentages. The age, height, weight, BMI, E-I, VR and Δ DBP of two groups were compared by independent Student's t test. A two-tailed ($\alpha=2$) p value less than 0.05 (p<0.05) was considered statistically significant. The subjects of two groups were demographically matched and thus, comparable.

Outcome measures-The expiration inspiration difference in terms of heart rate of two groups (CNDP and CDP) are summarized in Table II. Comparing the means of E-I, VR and

Ankita Grover, Department of Physiotherapy, SGT University, Gurugram, India

Richa Rai, Department of Physiotherapy, Banarsidas Chandiwala Institute of Physiotherapy, New Delhi, India

Priyanka Chugh Department of Physiotherapy, Banarsidas Chandiwala Institute of Physiotherapy, New Delhi, India

ΔDBP, t-test revealed non-significant differences between CDP group & CNDP group (p=0.288, p=0.728 and p=0.483 respectively).

when one or both parents are affected.¹⁵

Recently, it has been reported that cardiovascular diseases (CVD) and diabetes mellitus are quite prevalent in younger age group in developing countries, especially in Indian sub-continent. Diabetes and CVD share many common risk factors and the risk for mortality escalates with the co-occurrence of diabetes and CVD. Hence, early detection and treatment of diabetes, especially at a younger age is among the major strategies to prevent the occurrence of CVD in the general population.³¹ Previous studies have shown a sympathetic over activity in non diabetic insulin resistant subjects. Moreover, Laitinen et al., have identified an increased heart rate during acute hyperinsulinemia both, in insulin resistant and non insulin resistant offspring of type 2 diabetic subjects. However, De Angelis et al., have shown this condition at rest but not under stimulated conditions.^{16,17}

Heart rate response to Valsalva maneuver appears to be more sensitive parameter to detect autonomic dysfunction amongst the Parasympathetic function tests.^{18,19} According to ShirleyA Smith, reduced sinus arrhythmia at rest and during forced breathing appears to reflect cardiac vagal dysfunction.²⁰

It is known that impairment in vagal control of the heart usually precedes impairment in sympathetic cardiovascular regulation in diabetic patients and, indeed, arterial baroreflex control of sino atrial node has been reported to be altered early in the course of diabetic disease.¹⁴ As the subjects in our study were normal and quite young, the values obtained in the CANS testing may have thus come under normal limits, still keeping in mind the limitations of the study.

Our study showed insignificant blood pressure response to Sustained Hand Grip (p=0.483) in terms of mean diastolic pressure between CDP and CNDP group. In line with previous studies, we did not observe significant differences in cardiac autonomic modulation between CDP group and CNDP group. However, other studies have also detected a small but insignificant DBP fluctuation in CDP group than in CNDP group, which they presumed indicated an enhanced efferent sympathetic outflow to peripheral vasculature in CDPs, perhaps indicating the existence of a concomitant impairment in endothelial and ANS functioning in offspring of type2 diabetic patients, characterized by an enhanced peripheral sympathetic outflow, associated with an impairment of baro-reflex control of HR. They concluded that measures of primary prevention in such apparently normal, but higher risk population, targeted to both of these regulatory mechanisms, should be strongly recommended, which is also a suggestion of our study. Among these, a primary role may be played by regular physical activity, which has been demonstrated to improve both autonomic cardiovascular regulation and EF.²¹ In a recent study, Schroeder et al. also investigated the consequence of diabetes and pre-diabetic metabolic impairments.²²

The observations of certain studies indicate that subclinical autonomic neuropathy may develop without the presence of long term hyperglycaemia in family members of type 2 diabetic subjects³⁵. Different factors (including hyperglycaemia) could subsequently affect the expression of the genes and influence the progression of neuropathy. These

Table I: Basic characteristics (Mean ± SD) of two groups

Demographic Characteristics	CNDP (n=37) (%)	CDP (n=29) (%)	p value
Age (yrs)	20.5±1.5	21.2±1.8	0.067
Height (m)	163.2±7.6	163.6±7.2	0.827
Weight (kg)	56.6±8.3	57.8±9.4	0.586
BMI (kg/m ²)	21.2±1.8	21.5±2.5	0.502

Table II: Outcome measures (Mean ± SD) of two groups

Outcome measures	CNDP (n=37)	CDP (n=29)	p value
E-I (bpm)	39.1±7.8	36.9±8.7	0.288
VR	2.19±0.6	2.23±0.5	0.728
ΔDBP (mmHg)	33.2±14.4	35.8±15.9	0.483

IV. DISCUSSION

A great attention has been remunerated to describe the dynamics of physiological systems and on using them to distinguish healthy function from disease states. Much of this work has been investigated; how cardiovascular homeostasis, which is chief among them is maintained by multiple physiological control systems and the cardiac control by the autonomic nervous system (ANS) which can be assessed by the heart rate variability (HRV) signals. These signals carry information that reflect ongoing processes that normally go unnoticed, and help in diagnosis of incipient patho-physiological conditions before symptoms become obvious.¹⁴

Because T2DM and its complications are associated with considerable socioeconomic burden and mortality, there is increasing interest in developing strategies to prevent or delay progression of the disease. T2DM is attributed to both genetic and environmental factors. The growing number of new cases of young people being diagnosed with DM with co-morbid cardiac diseases has led to a thorough investigation and research studies regarding the risk factors for Type 2 diabetes mellitus (T2DM) in young adults. One of these risk factors is the positive family history of DM. Studies have estimated that the risk for T2DM increases approximately two- to-fourfold

results suggest that genetic factors could play a role in the pathogenesis of the features known as complications of type 2 diabetes, and they also suggest that these features can be present without diabetes being present clinically.^{14, 18, 21}

In parallel to our findings concerning autonomic neuropathy, other authors have suggested that subclinical autonomic neuropathy may be part of a genetic syndrome that includes augmented risk for developing cardiovascular disease (CVD), type 2 diabetes, symptomatic autonomic neuropathy, hypertension, and possibly premature death. Whether such development takes place could depend on exogenous factors, such as nutrition, smoking, and physical activity.^{23, 24, 25}

V. CLINICAL IMPLICATIONS

Studies have concluded that higher risk of type 2 Diabetes in first degree relatives indicated that some individuals have an inherited susceptibility to the development of disease.^{26, 27, 28} In our study, we had hypothesized variation in autonomic function tests can be assessed in normal non-diabetic healthy subjects who are susceptible to the condition which may/ may not get overt in later life, so that appropriate preventive and risk factor modification strategies / treatment measures can be undertaken.

Physiotherapists may thus play an important role in the society in reducing the stress levels and socioeconomic burden and increasing the physical activity level thus breaking the vicious cycle, by getting involved in the early diagnosis and preventive measures. Exercise training improves both autonomic function and exercise capacity.^{29, 30} However, our participants are still young and must be followed up for an early detection of subclinical autonomic dysfunction, as in subjects with diabetic history it is important for risk stratification and subsequent management, possibly including pharmacologic and lifestyle interventions.

VI. CONCLUSION

. On the basis of the results found in the present study, our null hypothesis (H_0) was accepted.

REFERENCES

- [1] Aaron I. Vinik and Dan Ziegler. Diabetic Cardiovascular Autonomic Neuropathy. American Heart Association. Circulation. 2007; 115:387-397.
- [2] American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2004 January; 27(1).
- [3] Schumer MP, Joyner SA, Pfeifer MA. Cardiovascular Autonomic Neuropathy Testing In Patients with Diabetes. DiabetSpectr 1998; 11: 227-223.
- [4] Mit Young Adult Development Project. <http://www.Hrweb.Mit.Edu/Worklife/Youngadult/Index-Html>.
- [5] Susan Jekiele and Brett Brown. A Kids Count/Prb/Child Trends Report On Census 2000 The Transition To Adulthood: Characteristics Of Young Adults Ages 18 To 24 In America. The Annie E. Casey Foundation, Population Reference Bureau and Child Trends, 2005 May.
- [6] Classification of Disease Risk Based On Body Mass Index (BMI). American College of Sports Medicine's Guidelines for Exercise Testing and Prescription. Edition 8th; 64.
- [7] Simran Grewal and Vidushi Gupta. Effect of Obesity on Autonomic Nervous System. Int J Cur Bio Med Sci 2011; 1(2): 15 – 18.
- [8] Pate RR Et Al and U.S. Department Of Health And Human Services. American College of Sports Medicine's Guidelines for Exercise Testing and Prescription. Edition 8th; 28.
- [9] Sudhir Modala1, QaziRais Ahmed, andSoudeep Kumar Saubarroso. Effect on Autonomic Nervous System in Smokers and Non Smokers- a Comparison study. National Journal of Medical and Allied Sciences 2012; 1(1):25-28.
- [10] Offried N. Niedermaier, Michael L. Smith, Larry A. Beightol, ZofiaZukowska-Grojec, David S. Goldstein and Dwain L. Eckberg. Influence Of Cigarette Smoking On human Autonomic Function. Circulation 1993 August; 88(2).
- [11] Thirumaran M, Balasubramanian K, Vishwanatha Rao B and Muralikrishnan. Heart Rate Variability Analysis in Alcohol Dependant Individuals Using Time Domain Measures. Sch. J. App. Med. Sci., 2013; 1(5):419-422.
- [12] AmritNanaiah, Sudipta D. Chowdhury, KanakamaniJeyaraman, and Nihal Thomas. Prevalence of Cardiac Autonomic Neuropathy in Asian Indian Patients with Fibrocalculous Pancreatic Diabetes. Indian J EndocrinolMetab. 2012 Sep-Oct; 16(5): 749-753.
- [13] C. Neumann and H. Schmid. Standardisation of a Computerised Method for Calculating Autonomic Function Test in Healthy Subjects and Patients with Diabetes Mellitus. Brazilian Journal of Medical and Biological Research 1997; 30:197-205.
- [14] DaadH.Akbar, MahaA.Hegazi, Hanan A. Al kadi. Possible Early Alteration Of Autonomic Activity Assessed By Heart Rate Variability in Saudi Offspring Of Type 2 Diabetic Patients. Saudi J Int Med 2011; 1(2):17-23.
- [15] Gang Chen, Meizhi Li, Yuan Xu et al. Impact of Family History of Diabetes On β -Cell Function and Insulin Resistance among Chinese with Normal Glucose Tolerance. Diabetes TechnolTher 2012 June; 14(6):463-468.
- [16] Tomi Laitinen, Ilkka K.J. Vauhkonen, Leo K. Niskanen, Juha E.K. Hartikainen, Esko A. Länsimies, Matti I.J. Uusitupa, And Markku Laakso.Power Spectral Analysis of Heart Rate variability during Hyperinsulinemia in Nondiabetic Offspring O F Type 2 Diabetic Patients Evidence for Possible Early Autonomic Dysfunction in Insulin-Resistant Subjects. Diabetes. 1999 June; 48.
- [17] De Angelis C, Perelli P, TrezzaR,Casagrande M, Biselli R, Pannitteri G Marino B, Farrace S. Modified Autonomic Balance In Offsprings Of DiaBetics Detected By Spectral Analysis Of Heart Rate Variability.Metabolism. 2001; 50:1270 –1274.
- [18] C. Hauerslev Foss, E. Vestbo, A. Frøland ,H.J. Gjessing, C.E. Mogensen and E.M.Damsgaard. Autonomic Neuropathy inNondiabetic Offspring of Type 2 DiabeticSubjects Is Associated with UrinaryAlbumin Excretion Rate and 24-hAmbulatory Blood Pressure. The FredericiaStudy. Diabetes.March 2001; 50(3):630- 636.
- [19] Sangeeta Tuppad and Swati Jangam. Relation between Weight, Height, Glycemic Status and Parasympathetic Functions In Nondiabetic Offspring Of Type 2 Diabetes Mellitus National Journal Of Medical Research. 2014 Jan; 4(1).
- [20] Shirley A Smith. Reduced Sinus Arrhythmia In Diabetic Autonomic Neuropathy: Diagnostic Value Of An Age-Related Normal Range. British Medical Journal 1982 December 4; 285.
- [21] Ferdinando Iellamo, ManfrediTesauro, Stefano Rizza, Stefano Aquilani, Carmine Cardillo,Micaelalantorno, Mario Turriziani Renato Lauro. Concomitant Impairment in Endothelial Function and Neural Cardiovascular Regulation in Offspring of Type 2 9diabetic Subjects. Hypertension published online Jul 24, 2006.
- [22] Emily B. Schroeder, Lloyd E. Chambless, et al. Diabetes, Glucose, Insulin, And Heart Rate Variability the Atherosclerosis Risk In Communities (ARIC) Diabetes Care 2005 March; 28(3):668-674.
- [23] Vinutha Shankar and ShivakumarVeeraiah. Age Related Changes in the Parasympathetic Control of the Heart.International Journal Of Scientific And Research Publications 2012June; 2(6),
- [24] SaheraShabnam S, Sridevi G and Sembulingam P. Gender Differences in Autonomic Functional Status in Response to Stress. Int J Med Res Health Sci. 2013; 2(4):737-44.
- [25] Hari Prasad T, Modala S, Baghal M, Et Al. Variation Of Autonomic Function Tests In Young Healthy Males And Females. International Journal of Information Research and Review. 2014; 1(3):73-75.
- [26] Wy So, Mcy Ng, Sc Lee and Tsanke. Genetics of Type 2 Dm.Hkmj2000; 6:69-76.
- [27] Barroso, I., Luan, J., Middelberg, R.P.S., Et Al. Candidate Gene Association Study in Type 2 Diabetes Indicates a Role for Genes Involved In B-Cell Function As Well As Insulin Action. PlosBiol, 2003. 1: 41-55.
- [28] Amruta Nitin Kumbhar and Lalit H Nikam. Cardiovascular autonomic response in children with parental history of diabetes mellitus: A comparative study. MedPulse – International Medical Journal, March 2015; 2 (3):181-186.

- [29] Z. Y. Fang, Johannes B. Prins, J. Sharman and Thomas H. Marwick. Determinants of Exercise Capacity in Patients with Type 2 Diabetes. *Diabetes Care* 2005; 28:1643–1648.
- [30] Loimaala A, HuikuriHv, Koobi T, Rinne M, Nenonen A and Vuori I: Exercise Training Improves Baroreflex Sensitivity In Type 2 Diabetes. *Diabetes* 2003; 52:1837–1842.
- [31] Autonomic Function Tests In Young Healthy Males And Females. *International Journal of Information Research and Review*. 2014; 1(3):73-75.
- [32] Wy So, Mcy Ng, Sc Lee and Tsanke. Genetics of Type 2 Dm.Hkmj2000; 6:69-76.
- [33] Barroso, I., Luan, J., Middelberg, R.P.S., Et Al. Candidate Gene Association Study in Type 2 Diabetes Indicates a Role for Genes Involved In B-Cell Function As Well As Insulin Action. *PlosBiol*, 2003. 1: 41-55.
- [34] Amruta Nitin Kumbhar and Lalit H Nikam. Cardiovascular autonomic response in children with parental history of diabetes mellitus: A comparative study. *MedPulse – International Medical Journal*, March 2015; 2 (3):181-186.
- [35] Z. Y. Fang, Johannes B. Prins, J. Sharman and Thomas H. Marwick. Determinants of Exercise Capacity in Patients with Type 2 Diabetes. *Diabetes Care* 2005; 28:1643–1648.
- [36] Loimaala A, HuikuriHv, Koobi T, Rinne M, Nenonen A and Vuori I: Exercise Training Improves Baroreflex Sensitivity In Type 2 Diabetes. *Diabetes* 2003; 52:1837–1842.



Dr. Ankita Grover
MPT, BPT

A cardiopulmonary physiotherapist, have completed masters with distinction in the same from Guru Gobind Singh Indraprastha University (GGSIPU), New Delhi and working as Assistant Professor in the department of Physiotherapy at SGT University.

Having experience in Adult cardiorespiratory care, cardiac and pulmonary rehabilitation, including exercise in the critically ill, pre and post-operative cases of cardiac surgery, including transplantation. Has expanded skills through previously working with Batra Hospital and Medical Research centre (BHMRC), New Delhi as consultant Physiotherapist specializing in ICU Rehabilitation, pulmonary rehabilitation, strength conditioning and endurance training. Had been working as Assistant Professor in Physiotherapy at Noida International University. Have attained CPR and AED Certification from Rashtriya Life Saving Society (RLSS), India. Also certified in Myofascial Physical therapy techniques and Sports first aid and on field management.

Having bagged 2nd prize in paper Titled “Correlation of health-related anthropometric measures with physical and motor fitness and proprioception in young collegiate females.” at NCPT, 2014

Successfully worked on a Dissertation titled “Correlation of health-related anthropometric measures with physical and motor fitness”.

Have also successfully carried out a research titled “Variation In Autonomic Function (CANS) Tests In Young Adults With And Without Parental History Of Diabetes Mellitus”.