ORIGINAL RESEARCH

The Study Of Autonomic And Respiratory Dysfunctions In Type 2 Diabetes Mellitus Subjects

Mohammad Shahid[1], Devendra Kumar Tripathi[2]

ABSTRACT

Background: Diabetes Mellitus is a metabolic disorder associated with malfunction of different organs, and its complications are mostly due to macrovascular and microvascular damage. Their is increased risk of cardiovascular mortality but the significance of Diabetic Autoneuropathy has not been fully studied. The presence of too much connective tissue and an extensive microvascular circulation in the lung raises the possibility that lung may be a 'target organ' in diabetic patients.
Material and Methods: Type 2 diabetes group (n=60) and control group (n=60). Cold pressor test, measurement of lung volumes by spirometer were done and two groups were compared.
Result: Basal heart rate and blood pressure were higher in the diabetic group than control group ($p<0.05$). A decreased response to cold pressor stress ($p<0.05$) was seen in diabetic group. Lung volumes were lower in diabetes group compared to the control group ($p<0.05$).
Conclusions: In diabetic group significant decrease in the blood pressure response seen to cold pressor test showing dysfunction in sympathetic activity. Even though type 2 diabetes patients did not have any respiratory symptoms but have underlying subclinical restrictive abnormality of lung functions.

Keywords: Diabetes mellitus, Autonomic neuropathy, Cold pressor test, lung volumes.

How to cite this article: Mohammad Shahid, Devendra Kumar Tripathi. The study of autonomic and respiratory dysfunctions in type 2 diabetes mellitus subjects. International Journal of Contemporary Medical Research 2015;2(3):561-565

Assistant Professor, [1]Department of Physiology, [2]Department of Medicine Rohilkhand medical college and Hospital, Bareilly, India.

Corresponding author: Dr. Mohammad Shahid, Assistant Professor, Department of Physiology, Rohilkhand medical college and Hospital, Bareilly, India.

Source of Support: Nil

Conflict of Interest: None

INTRODUCTION

Diabetes mellitus is defined as metabolic disorder which is characterized by chronic hyperglycemia with disturbances in metabolism of carbohydrate, fat, and protein which occur due to defects in insulin secretion and or insulin action.[1] Type 2 diabetes mellitus exerts a huge toll in human suffering and economy. It has been estimated that the global burden of T2DM for 2011 was 366 million people which is projected to increase to 552 million in 2030.[2] India is often referred as the diabetes capital of the world. For India, this increase is estimated to be 58%, from 51 million people in 2010 to 87 million in 2030.[3]
Although by definition, diabetes mellitus is characterized by elevated glucose concentrations, the impact of diabetes, resides almost entirely in the long term complications of diabetes affecting almost every system in the body including eyes, kidneys, heart, feet and nerves.[4]Diabetic neuropathy is one of the common complications of diabetes and specifically autonomic neuropathy can affect several systems with clinical manifestations more common in the cardiovascular, genitourinary, gastrointestinal and thermoregulatory systems. [5]Diabetic autonomic neuropathy frequently exists with other peripheral neuropathies and other diabetic complications, but DAN may be isolated, frequently preceding the detection of other complications.[6] Neuropathy is the most common complication of diabetes.[7] Neuropathy occurs more or less with the same frequency in both type 1 and type 2 diabetes, suggesting a common etiological mechanism based on chronic hyperglycemia.[8]Duchen and Coworkers attributed the autonomic disorder to vacuolization and inflammation of sympathetic ganglionic neurons, loss of myelinated fibres in the vagi and white rami communicantes and loss of lateral horn cells in the spinal cord.[9] Pathophysiological changes in the autonomic nervous syndrome were charecterized by diarrhea, bladder dysfunction, postural hypotension and signs and symptoms of cardiac denervation.[9] The prevalence of dysfunction in autonomic nervous system in diabetes cases were not studied extensively; but tests have shown impairment of autonomic function in nearly 20 - 30% of diabetic subjects.[10] Increased incidence of silent myocardial infarction, cardiac arrest, sudden

death, and inadequate response to stressful events has been noticed.[11] Recently, researchers consider the lung as a target organ in diabetes mellitus.[12,13] Many respiratory disturbances have been found with diabetes mellitus, including elastic recoil[14,15] reduced lung volumes, diminished respiratory muscle performance,[16] decrease in pulmonary diffusion capacity for carbon monoxide.[17,18] The pulmonary complications of diabetes mellitus is not well characterized. Some study had shown normal pulmonary function and other study had shown abnormal lung function test.[19,20] Present study was done to compare autonomic function tests between type 2 DM patients and non-diabetic controls and also to study pulmonary function tests between type 2 DM patients and non-diabetic controls.

MATERIAL AND METHODS

This study was cross sectional study and study was carried out in the Department of Physiology, Rohilkhand Medical College and Hospital, Bareilly.
The type 2 DM subjects were selected from OPD and IPD of medicine department. The clearance for study was taken from the ethical committee.The informed written consent was taken from the study group and a detailed clinical history was taken with each subject. The total sample size was 120 and they were divided into two group. The Group 1 is consist of 60 type 2 diabetes patients. Equal number of type2 diabetic male and female subjets were taken for study. The group 2 was the control group and consist of 60 healthy volunteers and were selected from the institution or patients attendants who are matched with non diabetic for age and gender. Diagnosis of Type 2 DM is done by either single raised glucose reading with symptoms, otherwise raised values on two occasions of either :Fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) or With a glucose tolerance test, two hours after the oral dose of plasma glucose ≥11.1 mmol/l (200 mg/dl).
Inclusion criteria: Those diagnosed cases of type 2 diabetes which had sufferd from disease for more than 5 years and they are non smokers.
Exclusion criteria: Patients of known cardiovascular illness like hypertension, Age above 60 and below 40 years, known chronic obstructive or restrictive lung disorders, Subjects with history of smoking/chronic drug intake, with gross abnormalities of thoracic cage, neuromuscular disease, cardiopulmonary disease or history of major thoracic surgery.Height (in cm) of the subjects was measured in standing and erect posture. Weight (in kg) was recorded using standard weighing machine in standing posture. Blood pressure, both systolic and diastolic, measured using mercury sphygmomanometer (in mm Hg) in right arm in sitting position. Resting pulse rate was recorded (in beats per minute). Mean blood pressure was obtained by adding diastolic pressure to one third of pulse pressure (in mm Hg). Cold pressure test was carried out using ice cold water, sphygmomanometer and stethoscope. Pulmonary function tests were carried out by using the computerized Spirometer Helios 401. Parameters recorded are FVC, FEV1, PEFR and FEV1/FVC ratio.

Methods of Cold pressor test

For this subjects pulse rate and blood pressure is measured first. Then the subjects hand is immersed in cold water, maintained at 4ºC and it is kept immersed upto a duration of 2 minutes. The subject is asked to relax, breathe quietly and avoid valsalva-like maneuver during the immersion. Blood pressure is measured using mercury sphygmomanometer on the opposite arm at forty-five seconds, ninety seconds and 2 minutes during the immersion.

STATISTICAL ANALYSIS

Mean and standard deviation were calculated by SPSS 17. Student independent ‘t’ test has been carried out to test the significance of mean.

RESULTS

For this cross sectional study, 60 diabetics and 60 controls between 40 to 60 years of age and with more than 5 years duration of disease were selected. The results obtained were expressed as Mean ± SD, statistical technique like independent t-test and ANOVA were used.The P value > 0.05 taken as Non significant (NS), <0.05 was taken significant(S) and <0.001 taken as (HS).

Groups	Height (meters)	Weight (Kgs)	BMI (kg/m2)
Diabetes	1.72 ± 0.06	65.66 ± 11.07	22.44 ± 3.24
Control	1.70 ± 0.08	65.22 ± 12.61	22.45 ± 3.19
P value	> 0.05, NS	> 0.05, NS	> 0.05, NS

Table-1: Anthropometric parameters of study subjects

Table 1 shows the comparision of the anthropometric parameters between diabetic case and their healthy matched control and results were expressed as Mean ± SD. There was no significant difference in height, weight and body mass index (BMI). Table-2 shows the comparision of the mean SBP and mean DBP

	Mean SBP		Significance	Mean DBP	Significance	Mean SBP
	Diabetes	Control	P value	Diabetes	Control	P value
Baseline	104 ± 12.77	114.11 ± 9.66	<0.001, HS	65.52 ± 6.11	68.60 ± 3.88	<0.001, HS
Ice water hand Immersion						
45 sec	105.44±11.76	120±106	<0.001, HS	65.66±6.98	73.44±6.55	<0.001, HS
90 sec	107.88±11.44	120.44±8.95	<0.001, HS	65.04±7.05	74.87±6.67	<0.001, HS
2 min	109.04±10.75	122.94±9.54	<0.001, HS	67.64±6.78	78.06±6.05	<0.001, HS

Table-2: Comparison of mean blood pressure during the cold pressor test

parameters between diabetes cases and their healthy matched control and results were expressed as Mean ± SD.

There was highly significant difference in mean SBP and mean DBP in basal condition and after ice water hand immersion at different intervals. Table 3 shows the comparisionof the resting HR, SBP, DBP and MBP between diabetic case and their healthy matched control and results were expressed as Mean ± SD. There was no significant difference in resting HR between diabetic cases and their control but their was highly significant difference in basal SBP, DBP and MBP between diabetic and control. Table 4 shows the comparision of the PFT paremeters between diabetes case and their healthy matched control and results were expressed as Mean ± SD. There was no significant difference in mean FEV1/FVC, mean PEFR between diabetic case and their control but their was highly significant difference in mean FVC and mean FEV1 between diabetes and their control.

Parameters	Diabetes	Controls	P value
Resting heart rate	78.05± 4.45	74.35± 8.76	<0.05, S
Systolic blood pressure	106 ± 11.66	114.28 ± 9.44	<0.001, HS
Diastolic blood pressure	64.98 ± 6.75	68.05 ± 4.22	<0.001, HS
Mean blood pressure	78.66 ± 7.45	84.22 ± 5.05	<0.001, HS

Table-3: Comparison of cardiovascular parameters

Parameters	Diabetes	Control	P value
Mean FVC	77.44±17.98	94.44±11.87	<0.001, HS
Mean FEV1	85.05±15.99	99.66±17.08	<0.001, HS
Mean FEV1/FVC	111.44±6.56	109.02±12.06	>0.05, NS
Mean PEFR	81.86±17.43	85.77±16.45	>0.05, NS

Table-4: Comparison of lung volumes between the groups

DISCUSSION

In present study there were no significant differences in anthropometric parameters between the diabetic and control groups. The variation of blood pressure both systolic and diastolic after exposure to the ice cold water compared to the baseline blood pressure readings taken before immersion shows significance in diabetes group compared to controls. The maximum variation in the SBP was seen at 2 min after immersion in compare to control group. The diastolic blood pressure change in diabetics at 2 min after immersion shows significance compared to the control group. It also shows a significant change in difference from the baseline of the systolic and diastolic blood pressure throughout the ice immersion of cold pressor test. Similarly, Nitenberget al.,[21] in their study concluded that in diabetic patients, response to sympathetic activation elicited by a cold pressor test is often altered and predicts major cardiac events.Immersion of hand in cold water produced a marked increase in HR, SBP and DBP. These changes can be explained on the basis of increased sympathetic activity with release of nor epinephrine and epinephrine.[22] In our study there was a significant decrease in the level of FVC and FEV1 in diabetics compared to controls whereas no significant change FEV1/FVC and PEFR were found. Similar study was done by Meo SA et al.[23,24] Anand R et al.,[25] studied that all respiratory parameters and showed significant reduction. . Gouher BS et al.,[26] in their study showed that PEFR and MEP were reduced in type2 diabetic patients compared to control. In our study level of FVC and FEV1 decreased while FEV1 /FVC showed increase but PEFR showed no significant change with more than five year duration of diabetes. Similarly, Meo et al.[27] study found significant reduction in FVC of duration of 5–12 years. Lawlor DA et al.,[28] in their cross-sectional study to assess the associations of lung function with insulin resistance and Type 2 diabetes and concluded that FEV1 and FVC were inversely associated with insulin resistance and prevalence of Type 2 diabetes whereas, Davis et al., [29] studied that FVC, FEV1, VC and PEF were decreased in diabetic patients. In our study, PEFR was reduced but not significantly. Similarly, in a study by Kanya KDH et

al.,[30] no change in PEFR values in diabetics was observed as the duration of diabetes increased indicative for restrictive pattern.

Significant decrease in the means of resting heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure and pulse pressure seen in the diabetes group compared to control group. As explained earlier in diabetes there is impaired sympathetic and parasympathetic outflow to the heart. This leads to increased resting heart rate and decreased resting blood pressure.The present study also suggests that type 2 diabetes mellitus adversely affects the pulmonary function, and results are in line with other previously conducted studies also, the study demonstrated a correlation between the duration of disease and the decline in lung function.

CONCLUSION

Evaluation of autonomic functions as cardiovascular reflexes in type 2 DM subjects with silence of related symptoms constitutes an important feasible and reproducible bedside clinical technique. It should be included as a routine in the work-up of patients of type-2 diabetes as it often uncovers autonomic neuropathy even in the asymptomatic state. It is of crucial importance to look after some high-risk cases with probability of sudden cardiac death. It is also to look upon a search for other complications of diabetes often associated with it. Even though type 2 diabetic patients did not have any respiratory symptoms they did have mild restrictive patterns of lung functions. The type 2 diabetes mellitus subjects were found to have restrictive pattern of respiratory abnormality. Spirometry is a simple non-invasive diagnostic tool and cost effective and it use can give signal to take early preventive measures in tpe2 DM subjects.

REFERENCES

1. Khaled AA, Sekaran M, Ikram SI. Type 2 Diabetes and Vascular Complications: A pathophysiologic view. Biomedical Research 2010;21:147-55.
2. International Diabetes Federation.Diabetes Atlas, fifth edition. International Diabetes Federation, Brussels; 2011.
3. Snehalatha and Ramachnadaran 2009, Insight into the Mechanism of Primary Prevention of Type 2 Diabetes: Improvement in Insulin Sensitivity and Beta cell function. Genetic and Epigenetic Basis of Complex Diseases. Conference in Centre for Cellular and Molecular Biology; December, 2009.
4. Jayaram B M et al. Type 2 Diabetes Mellitus and its complications: A preventive program 2008.
5. Kennedy WR, Navarro X, Sakuta M, Mandell H, Kox CK and Sutherland DE. Physiological and clinical correlates of cardiorespiratory reflexes in diabetes mellitus. Diabetes Care 1989;12:399-408.
6. Vinik AI, Maser ER, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. Diabetes Care 2003; 26:1553-79.
7. Maser RE, lenhard MJ. Cardiovascular autonomic neuropathy due to diabetes mellitus: clinical manifestations, consequences and treatment. Journal of Clinical Endocrinology and Metabolism 2005;90:5896-903.
8. Malecki MT, Klupa T. Type 2 diabetes mellitus: from genes to disease. Pharmacological Reports 2005;57:20-32.
9. Duchen LW, Anjorin A, Watkins PJ, Mackay JD. Pathology of autonomic neuropathy in DM. Ann. intern. Med 1980;92:301.
10. Basu AK, Bandyopadhyay R, Chakrabarti S, Paul R, Santra S. A study on the prevalence of cardiac autonomic neuropathy in type-2 diabetes in Eastern India. JIACM 2011;13:22-6.
11. Maser RE, Pfeifer MA, Dorman JS, Kuller et al. Diabetic Autonomic Neuropathy and Cardiovascular Risk: Pittsburgh Epidemiology of Diabetes Complications StudyIII. Arch Intern Med 1990; 150:1218-22.
12. Sandler M. Is the lung a 'target organ' in diabetes mellitus. Arch Intern Med 1990; 150(7):1385-8.
13. Sandler M. Is the lung a target organ in diabetes mellitus? Arch Intern Med. 1990;150:1385–88.
14. Sandler M, Bunn AE, Stewart RI. Cross-section study of pulmonary function in patients with insulin dependent diabetes mellitus. Am Rev Respir Dis 1987;135:223-9
15. Schulyler M, Niewoehner D, Inkley S, Kohn R: Abnormal lung elasticity in juvenile diabetes mellitus. Am Rev Resp Dis 1976;113:37-41.
16. Wenke T, Formanek D, Auinger M, et al: Inspiratory muscle performance and pulmonary function changes in IDDM. Am Rev Respir Dis 1991;143:97-100.
17. Cooper BG, Taylor R, Albert GMM. Lung function in patients with diabetes mellitus. Respir Med 1990;84:235-9.
18. Maccioni FJ, Colebatch HJ. Lung volumes and distensibility in insulin dependent diabetes mellitus. Am Rev Respir Dis 1991;143:1253-6.
19. Meo SA, Al-Drees AM, Shah SF, Arif M, Al-R K. Lung function in type1 Saudi diabetic patients.Saudi Med J 2005 Nov;26(11):1728-33.
20. Meo SA, Al-Drees AM, Arif M, Al-Rubean K. Lung function in type 2 Saudi diabetic patients. Saudi Med J 2006 Mar;27:338-43.
21. Nitenberg A, Valensi P, Sachs R et al. Prognostic value of epicardial coronary artery constriction to the cold pressor test in type 2 diabetic patients with angiographically normal coronary arteries

and no other major coronary risk factors. Diabetes Care 2004;27:208–15.
22. Fagius J, Karhuvaara SG. The cold pressor test: effects on sympathetic nerve activity in human muscle and skin nerve fascicles. Acta Physiologica Scandinavi 1989;137:325-34.
23. Meo SA, Al-Drees AM, Shah SF, Arif M, Al-Rubean K. Lung function in type 1 Saudi diabetic patients. Saudi Med J 2005;26:1728-33.
24. Meo SA, Al-Drees AM, Arif M, Al-Rubean K. Lung function in type 2 Saudi diabetic patients. Saudi Med J 2006;27:338-43.
25. Anand R. Dharwadkar, Asha A. Dharwadkar, Gouher B, Shrilaxmi B. Reduction In Lung Functions In Type-2 Diabetes In Indian Population : Correlation With Glycemic Status. Indian J PhysiolPharmacol 2011;55:170–5.
26. Gouher BS, Anita D, Pallavi K, Lata M, Manjunatha A. A comparative study of lung functions in type-2 diabetes and non diabetic subjects. IJBAR 2012;03:629-31.
27. Meo SA, Al-Drees AM, Ahmed J, Shah SF, Al-Regaiey K, Al-Rubean K et al. Effect of Duration of Disease on Ventilatory Function in an Ethnic Saudi Group of Diabetic Patients. J Diabetes SciTechnol 2007;1:711-7.
28. Lawlor DA, Ebrahim S, Smith GD. Associations of measures of lung function with insulin resistance and Type 2 diabetes: findings from the British Women's Heart and Health Study. Diabetologia 2004;47:195–203.
29. Davis Timothy ME, Mathew Knuimann, Peter Kendall. Reduced pulmonary function and its association in type-2 Diabetes. Diabetes Research and Clinical Practice 2000;50:152-9.
30. Kanya KDH, Nataraj SM, Devaraj HS. Correlation of duration of diabetes and pulmonary function tests in type 2 diabetes mellitus patients. Int J Biol Med Res 2011;2:1168-70.