



PULMONARY FUNCTION TESTS IN PREDIABETES.

Dr.Sandeep.S

Postgraduate, Department of Physiology, Coimbatore Medical College,

Dr.R.Shanmughav
adivu*Professor & Head of Department, Department of Physiology, Coimbatore Medical
College,*Corresponding Author

ABSTRACT **BACKGROUND:** Diabetes mellitus (DM) is the most common metabolic disorder which is on increasing trend globally. Studies have suggested that impaired lung function is a complication of diabetes mellitus. However, no study has examined the association between prediabetes and lung function in our Indian population. Therefore we took the study to find out the association between lung function and prediabetes. **AIM:** To assess the pulmonary function in prediabetes. **MATERIALS & METHODS:** This is a case-control study involving 50 cases with prediabetics and 50 age and sex matched controls meeting inclusion criteria. Blood investigations including fasting blood glucose and postprandial blood glucose and pulmonary function tests using computerized spirometer were done in both the cases and controls. **RESULTS:** The mean value of Forced Vital Capacity (FVC), Forced Expiratory Volume1 (FEV1) & FEV1/ FVC in prediabetics are 2.97 ± 0.43 , 2.51 ± 0.34 & 0.81 ± 0.05 respectively which was lower than Forced Vital Capacity (FVC), Forced Expiratory Volume1 (FEV1) & FEV1/ FVC of normoglycemic subjects which is 3.16 ± 0.26 , 2.54 ± 0.28 & 0.85 ± 0.12 respectively. **CONCLUSION:** Our study showed that prediabetics have reduced pulmonary functions compared to normoglycemic subjects which was of restrictive pattern. Hence it is important to do periodic lung function test in prediabetics for early detection of lung abnormalities.

KEYWORDS : Diabetes mellitus (DM), Forced Vital Capacity (FVC), Forced Expiratory Volume1 (FEV1), Prediabetes.

INTRODUCTION:

Diabetes Mellitus (DM) is the most common metabolic disorder which is on increasing trend globally. According to International Diabetes Federation, in addition to the 415 million adults who are estimated to currently have diabetes mellitus, there are 318 million adults with impaired glucose tolerance (IGT), which puts them at high risk of developing the disease in the future. India is the second largest contributor of diabetes mellitus in the World with 69.2 million and 2040 projection estimates of 123.5 million, second only to China. India is already the largest contributor of IGT in the world with 36.5 million population affected with IGT in 2015.(1)The Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) national study reported that there are 62.4 million people with type 2 diabetes mellitus and 77 million people with pre-diabetes in India.(2)

Prediabetes is the precursor stage to Type 2 Diabetes Mellitus which is defined by American Diabetes Association (ADA) as impaired fasting glucose (IFG) of 100–125 mg/dl (5.6–6.9 mmol/l) or IGT of 140–199 mg/dl (7.8–11.0 mmol/l) after two hours postprandial.(3) Prediabetes is not only associated with increased risk of progression to T2DM but also with increased cardiovascular disease (CVD) risk.(4)Current consensus definition of metabolic syndrome incorporates hyperglycemia, obesity, hypertension, hypertriglyceridemia and reduced high density lipoprotein cholesterol (HDL-C).(5) However, many researchers believe that insulin resistance is the core pathophysiology which mediates metabolic syndrome.(6)

Diabetes mellitus (DM) leads to microvascular and macrovascular complications which results in many of the systemic functional derangements. Diabetes mellitus causes glycosylation of alveolar-capillary proteins leading to microangiopathy in the lungs. Experimental studies on lung tissue from diabetic rats, autopsy and transbronchial biopsy studies in a few diabetics confirmed this hypothesis. Patients with DM had increased thickness of the alveolar capillary and bronchial-capillary basement membranes. These biological changes translate into clinical findings such as impairment in pulmonary functions.(7)

Studies have suggested that impaired lung function is a complication of diabetes mellitus. However, no study has examined the association between prediabetes and impaired lung function in our Indian population. Therefore we took the study to find out the association between lung function and prediabetes.

AIM: To evaluate the pulmonary function in prediabetics.

OBJECTIVES OF THE STUDY

- To measure the fasting and post prandial plasma glucose level and there by diagnose the people with prediabetes.

- To measure Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1) and FEV1/FVC in prediabetics and in normal subjects.
- To correlate the pulmonary function tests parameters with the plasma glucose values.

MATERIALS & METHODS:

After getting an approval from the Institutional Human Ethical Committee, this study was conducted in the Department of Master health-check-up, Coimbatore medical college and hospital. This study was carried out from October-2019 to December-2019 for a period of three months. Informed and written consent was obtained from the subjects. Pre-procedure assessment including history, general examination, and systemic examination was done. Baseline vitals were recorded.

Blood investigations including fasting blood glucose and postprandial blood glucose were done in the subjects. This is a case-control study involving 50 cases who are diagnosed to have prediabetes and 50 age and sex matched normal subjects are taken as controls.

Inclusion criteria:

- Age – 25 to 60 years of age.
- Cases - 50 prediabetics with,
 - Impaired Fasting Glucose (IFG) – Fasting plasma glucose levels of 100-125mg/dl.
 - Impaired Glucose Tolerance (IGT) – Postprandial glucose levels of 140-199mg/dl.
- Controls -50 age and sex matched normal subjects.

Exclusion criteria:

- Smokers.
- History of any lung diseases such as asthma or any other COPD.
- Tobacco users.
- Deformities of chest wall or spine
- History of or symptoms of any neuromuscular disorders
- Hypertensive patients.
- Those with severe or communicable lung infections like tuberculosis.

The procedure of Pulmonary Function Test (PFT) was explained to the subject in his own language. Pulmonary function tests using computerized spirometer were done in both the cases and controls. Various PFT parameters such as: FEV 1, FVC, FEV 1/ FVC were recorded and studied.

STATISTICAL ANALYSIS:

Statistical analysis was performed using descriptive statistics and inferential statistics using student's independent t-test. The data was analysed using the SPSS (Statistical Package for Social Science) software version 20.0. A P value of <0.05 was considered as a level of significance.

RESULTS:

The study group included 50 prediabetics and control group included 50 healthy controls. In our study we found that Prediabetic patients have significantly lesser values of Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1) and FEV1/FVC as compared to normoglycemic subjects as tabulated as follows,

PFT Parameter	Controls (n=50)	Cases (n=50)	Mean difference	p value
FVC (litres)	3.16±0.26	2.97 ±0.43	0.19	0.012*
FEV1 (litres)	2.54±0.28	2.51±0.34	0.03	0.010*
FEV1/FVC	0.85±0.12	0.81±0.05	0.04	0.010*

FVC - Forced Vital Capacity; FEV1 - Forced Expiratory Volume in 1 second. *p value – statistically significant

DISCUSSION:

In our study we found that prediabetics had reduced lung function compared to normoglycemic subjects. FVC, FEV1 & FEV1/FVC ratio were statistically significantly lower in prediabetic patients than in normal controls (p<0.05). Also the prediabetics have restrictive pattern of lung disease compared to normoglycemic subjects. The reduced lung function probably is due to chronic high level of circulating glucose which cause an increase in non-enzymatic glycation of proteins and peptides in the pulmonary extracellular matrix as in diabetes mellitus.

Similarly, researchers have found that the risk for the development of diabetes mellitus is more in subjects with increased IGT (Impaired Glucose Tolerance) and with Low lung volume. They also state that IGT, was significantly associated with reduced lung volume and not IFG (Impaired Fasting Glucose).

Diabetes mellitus is a disease which leads to microvascular and macrovascular complications resulting in multisystem dysfunction. These microvascular changes in lung tissue will lead to impairment in pulmonary functions. Few studies have shown that T2DM with microangiopathies show reduced diffusion capacity for carbon monoxide (DLCO). The study further suggested that hyperglycaemia and dyslipidemia might have a contributory role in its pathogenesis.

Studies suggested that collagen and elastin changes seen in diabetic patients could be attributed to the small vessel involvement which may eventually lead to significant structural changes. A chronic high level of circulating glucose is also believed to cause an increase in non-enzymatic glycation of proteins and peptides in the pulmonary extracellular matrix. These factors may be involved in the pathological changes of the pulmonary parenchyma of T2DM patients. Some studies state that chronic low grade tissue inflammation along with microangiopathy and accumulation of advanced glycation end products can result in lung restriction in diabetes mellitus finally leading to diabetic morbidity and mortality.

Yeh HC et al have suggested that a PFT test in middle aged non-diabetic adult showing a restrictive pattern of lung pathology is predictive of subsequent type 2 diabetes mellitus. Hsin-Chieh Yeh et al, in their study have found that reduced vital capacity independently predicts the onset of type 2 diabetes mellitus. It is also suggested that vital capacity be considered as an important risk factor for developing insulin resistance and diabetes mellitus. Bruce B. Duncan et al have found in their study that an increase in levels of interleukin-6 signifying a low-grade inflammation may predict an impending onset of type 2 diabetes mellitus.

Connie C.W. Hsia has stated that moderate lung restriction is seen in type 2 diabetes mellitus as in type 1 diabetes mellitus. FVC and FEV1 are proportionately reduced as the increase in glycemic levels and loss of lung diffusing capacity (DLCO). (14) The Copenhagen City Heart Study done over 15 years showed that there was consistently lower (FEV1) and (FVC) in diabetics compared to normal individuals. (15) Muhammad Irfan et al., studied PFT in diabetics and showed that there was a significant reduction in forced vital capacity (FVC), FEV1 and

low vital capacity. They also studied that impaired lung function was independent of smoking and is likely to be a complication of diabetes mellitus itself (16) Research done by Wendy A. Davis et al., showed that reduced lung volumes are the result of chronic complications of DM and is related to glycemic exposure. They also revealed that airflow limitation is a predictor of mortality. (17)

David A. Kaminsky has opined that lung function is an important marker of increased risk of mortality in diabetic patients. Further, it is suggested that low FEV1 is a marker of diabetes mellitus or poor glycemic control, hence it is better to add the spirometer to the equipments available for monitoring the control of diabetes mellitus and its important complications. (18)

CONCLUSION:

Our study showed that prediabetics have reduced pulmonary functions compared to normoglycemic subjects which was of restrictive pattern. Pulmonary function impairment leads to decreased physical working capacity in diabetics. Since majority of the work force in our country is in 30s and 40s age group, the pulmonary dysfunction in the early years could affect productivity drastically at both individual and community levels. Hence it is important to do periodic lung function test in prediabetics for early detection of lung abnormalities.

REFERENCES:

- Gan D, King H, Lefebvre P, Mbanya J-C, Silink M, Siminerio L, et al. Diabetes Atlas Second Edition. In: International Diabetes Federation IDF Diabetes Atlas [Internet]. 2015 [cited 2020 Mar 1]. Available from: www.idf.org
- Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian Council of Medical Research-India DIABetes (ICMR-INDIAB) study. *Diabetologia*. 2011;54(12):3022–7.
- Genuth S, Alberti KGMM, Bennett P, Buse J, DeFronzo R, Kahn R, et al. Follow-up Report on the Diagnosis of Diabetes Mellitus. Vol. 26, *Diabetes Care*. 2003. p. 3160–7.
- Ford ES, Zhao G, Li C. Pre-Diabetes and the Risk for Cardiovascular Disease. A Systematic Review of the Evidence. *J Am Coll Cardiol* [Internet]. 2010 Mar 30 [cited 2020 Mar 1];55(13):1310–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20338491>
- Grundt SM, Cleeman JJ, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Vol. 112, *Circulation*. 2005. p. 2735–52.
- Reaven GM. Insulin resistance, the insulin resistance syndrome, and cardiovascular disease. Vol. 47, *Panminerva Medica*. 2005. p. 201–10.
- Weynand B, Jonckheere A, Frans A, Rahier J. Diabetes mellitus induces a thickening of the pulmonary basal lamina. *Respiration* [Internet]. 1999 [cited 2020 Mar 1];66(1):14–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9973685>
- Chance WW, Rhee C, Yilmaz C, Dane DM, Pruneda ML, Raskin P, et al. Diminished alveolar microvascular reserves in type 2 diabetes reflect systemic microangiopathy. *Diabetes Care*. 2008 Aug;31(8):1596–601.
- Sinha S, Guleria R, Misra A, Pandey RM, Yadav R, Tiwari S. Pulmonary functions in patients with type 2 diabetes mellitus & correlation with anthropometry & microvascular complications. *Indian J Med Res*. 2004 Feb;119(2):66–71.
- Mori H, Okubo M, Okamura M, Yamane K, Kado S, Egusa G, et al. Abnormalities of Pulmonary Function in Patients with Non-insulin-Dependent Diabetes Mellitus. *Intern Med*. 1992 Feb;31(2):189–93. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/1600265>
- Yeh HC, Punjabi NM, Wang NY, Pankow JS, Duncan BB, Brancati FL. Vital capacity as a predictor of incident type 2 diabetes: The Atherosclerosis Risk in Communities Study. *Diabetes Care* [Internet]. 2005 Jun;28(6):1472–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15920070>
- Yamane T, Yokoyama A, Kitahara Y, Miyamoto S, Haruta Y, Hattori N, et al. Cross-sectional and prospective study of the association between lung function and prediabetes. *BMJ Open* [Internet]. 2013;3:2179. Available from: <http://bmjopen.bmj.com>
- Duncan BB, Schmidt MI, Pankow JS, Ballantyne CM, Couper D, Vigo A, et al. Low-grade systemic inflammation and the development of type 2 diabetes: The atherosclerosis risk in communities study. *Diabetes* [Internet]. 2003 [cited 2020 Mar 2];52(7):1799–805. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/12829649>
- Mori H, Okubo M, Okamura M, Yamane K. Abnormalities of pulmonary function in patients with non-insulin-dependent diabetes mellitus. *Intern Med* 1992 Feb;31(2):189–93.
- Duncan BB, Schmidt MI, Pankow JS, Ballantyne CM, Couper D, and Vigo A. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. *Diabetes* 2003 Jul; 52(7):1799-805.
- Irfan MI, Jabbar A, Haque AS, Awan S, Hussain SF. Pulmonary functions in patients with diabetes mellitus. *Lung India* 2011 Apr; 28(2):89-92.
- Davis WA, Knuiman M, Kendall P, Grange V, Davis TM. Glycemic Exposure Is Associated with Reduced Pulmonary Function in Type 2 Diabetes: the Fremantle Diabetes Study. *Diabetes Care* 2004 March; 27(3):752-7.
- David A. Kaminsky. Spirometry and Diabetes: Implications of reduced lung function. *Diabetes Care* 2004 Mar; 27(3):837-8.