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Original Research Article

Assessment of pulmonary function test in type 2 diabetes mellitus and its correlation with their HbA1c levels

Archana Toppo, Kulvant Singh Ajamani*

Department of Medicine, Pt. J.N.M. Medical College, Dr. B.R.A.M Hospital, Raipur, Chhattisgarh, India

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***Correspondence:**
Dr. Kulvant Singh Ajamani,
E-mail: bhagatgreat@gmail.com

ABSTRACT

Background: Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia and deranged metabolism of carbohydrates, lipids and protein that result from insensitivity to endogenous insulin. It is a substantial global health problem and markedly increases morbidity and mortality of the affected people.
Methods: The present study was conducted in the Department of medicine Dr. B.R.A.M. Hospital, Raipur. Total 67 subjects with type II diabetes mellitus as per WHO criteria of diabetes mellitus, aged between 18-60years of both sexes were included in the study. Patients FBS, PPBS were analysed by glucose oxidase (GOD), peroxidase (POD) methods in ILAB 650 analyser and HbA1C was analysed using HPLC. Pulmonary function test was conducted in all the subjects using the spirometer which is the gold standard for accurate and repeatable measurement of lung function.
Results: Majority of the subjects were male (36, 53.7%) and belonged to age group of 51-60years (n=34, 50.7%), Duration of DM </=10years (n=47, 70.1%), restrictive pulmonary function in 10 (14.9%) subjects. Correlation of age with a restrictive pattern of PFT (P=0.013*) and with duration of diabetes (P<0.0001**). Pulmonary function test parameters having mild downstream correlation with diabetes mellitus.
Conclusions: Diabetes was more common in the sixth decade of life with slight male preponderance. The short-term indicators of glycaemic controls were not significantly associated with a restrictive pattern of PFT. Despite the best effort, there are limitations of this study, which includes small sample size, author have not taken general population, and lack of a control group. These limitations can be overcome in the future studies.

Keywords: Diabetes mellitus, HbA1c, Pulmonary function test

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia and deranged metabolism of carbohydrates, lipids and protein that result from insensitivity to endogenous insulin.[1] It is increasing in epidemic proportions throughout the world and positioned a significant economic burden over them. It is a substantial global health problem and markedly increases morbidity and mortality of the affected people.[2] As per the International Diabetes Federation prediction, in 2014 at least 387million people were living with diabetes mellitus and by the year 2035, this number will climb to almost 600million people, thus affecting more than one in 10 adults worldwide. The overall prevalence of diabetes in all the 15 states of India was 7.3%. There is a higher prevalence of diabetes in low SES groups in the urban areas of the more economically developed states of India.[3] As a metabolic disorder, diabetes is accompanied by widespread biochemical, morphological and functional abnormalities and affects nearly all systems in the human body. The complications resulting from the

disease are a significant cause of morbidity and mortality and are associated with the damage or failure of various organs such as the eyes, kidneys and nerves. Individuals with type 2 diabetes are also at a significantly higher risk for coronary heart disease, peripheral vascular disease, stroke and they have a greater likelihood of having hypertension, dyslipidemia, and obesity.[1] Type 2 diabetes mellitus is associated with the development of microvascular and macrovascular complications.[4]

The development of these complications can be explained by the biochemical adjustment in connective tissue as well as by microangiopathy due to protein glycosylation induced by chronic hyperglycemia.[5] Macrovascular complications lead to a spectrum of cardiovascular disease to which accelerated atherosclerosis is usually a contributor. The risk of cardiovascular diseases is doubled in diabetes mellitus.[6] The macrovascular complications of diabetes mellitus include coronary artery disease (leading to ischemic heart disease-angina and myocardial infarction), peripheral vascular disease (leading to intermittent claudication and diabetic foot), diabetic myonecrosis and strokes.[7] The microvascular changes result in diabetic retinopathy, diabetic nephropathy, diabetic neuropathy and diabetic cardiomyopathy.[8] Chronic hyperglycemia in diabetes may lead to systemic inflammation which results in airway and lung damage.[9] As a proinflammatory stimulus, chronic hyperglycemia leads to increased intrapulmonary inflammation and tissue fibrosis. Structural modifications of the lung parenchyma that result from these changes include the narrowing of the alveolar space, flattening of the alveolar epithelium and expansion of the interstitial.

The result is a reduction of lung volumes and pulmonary diffusion capacity.[10] T2DM individuals are known to have reduced exercise capacity and the level of reduction is associated with diabetes control. The pulmonary and other late complications of diabetes share a similar microangiopathy mechanism. Since, they share common mechanisms, there may be associations between lung function and markers of microangiopathy.[11]

The association between pulmonary function in T2DM and duration of diabetes, adequacy of glycemic control and body composition is inconclusive. Some studies have concluded that impaired lung function is negatively associated with impaired glycemic status and duration of diabetes.[12] Few studies showed that DM is associated with statistically significant, impaired pulmonary function in a restrictive pattern but these results were irrespective of body mass index (BMI), smoking, duration of diabetes and HbA1c levels.[13]

Although a lot of research work is being carried out on the prevalence of chronic complications of T2DM worldwide, there is a dearth of information in literature pertaining to the prevalence of impaired lung function in people with T2DM. Globally, the association between indices of microvascular disease and lung function in T2DM are also not extensively studied. Present study is a relevant step towards the future to overcome the lacuna in this field with the aim to measure pulmonary function tests in patients of diabetes mellitus and to correlate HbA1c levels of these patients with various parameters of pulmonary function tests. The results of this study will help bridge the knowledge gap and provide population relevant data on the pulmonary function and related factors in T2DM.

METHODS

This was a hospital-based cross-sectional observational analytical study conducted in the Department of Medicine, Pt. JNM Medical College, Dr. B.R.A.M. Hospital Raipur among the patients presenting in OPD and admitted in medicine ward or intensive care unit from the period between June 2016 to May 2017.

Total 67 subjects with type II diabetes mellitus as per WHO criteria of diabetes mellitus (fasting blood glucose of >126mg/dl and postprandial two hrs. blood glucose of >140mg/dl), aged between 18-60years of both sexes, who gave informed consent were included in the study.

Patients with complaints of a cough, sputum, or dyspnea, history of smoking, any ischemic and valvular heart disease, with chronic occupational exposure and deformities as kyphoscoliosis were excluded from this study.

The institutional ethics committee of Pt. JNM Medical College Raipur, Chhattisgarh, approved this study protocol. Informed written consent was obtained from all study participants. Subject's brief history of the condition was sought and detailed clinical examination was performed. Patients FBS, PPBS were analyzed by glucose oxidase (GOD), peroxidase (POD) methods in ILAB 650 analyzer and HbA1C was analyzed using HPLC. Pulmonary function test was conducted in all the subjects using the spirometer which was the gold standard for accurate and repeatable measurement of lung function.

Data were expressed as a percentage and mean±SD. Student's t-test was used to check the significance of the difference between two parameters in parametric data. Pearson correlation analysis was performed to check the correlation between two categorical variables. Fischer's exact test or Chi-square test was used to analyze the significance of the difference between frequency distribution of the data. A p-value <0.05 was considered as statistically significant.

RESULTS

The present study was conducted in the Department of Medicine Dr. B.R.A.M. Hospital, Raipur and included 67 subjects with diabetes mellitus presenting to OPD or inpatient wards from June 2016 to October 2017.

Majority of the study subjects belonged to the age group of 51-60years (n=34, 50.7%) followed by age group of 41-50years (n=23, 34.3%) with mean age of 50.3±7.14years. Majority of the subjects were male (36, 53.7%) (Table 1). The mean FBS was 114.8±17.5mg/dl while mean PPBS was 151.6±23.8mg/dl (Figure 1).

Table 1: Age and gender distribution in study subjects.

Variables		Frequency (n)	%
Age (years)	</=40	10	14.9
	41-50	23	34.3
	51-60	34	50.7
Gender	F	31	46.3
	M	36	53.7

Most of the subject having abnormal high HbA1c (n=48, 71.6%). A large population of subjects having duration of DM </=10years (n=47, 70.1%) while n=20 (29.9%) subject having diabetes for >20years.

Majority of the subjects having normal BMI (n=47, 70.1%) and normal pulmonary function (n=57, 85.1%). The restrictive pulmonary function was found in 10 (14.9%) subjects (Table 2).

The age was significantly higher (P=0.013*) in subjects with a restrictive pattern of PFT and the duration of diabetes was significantly longer in restrictive pulmonary function pattern (P<0.0001**).

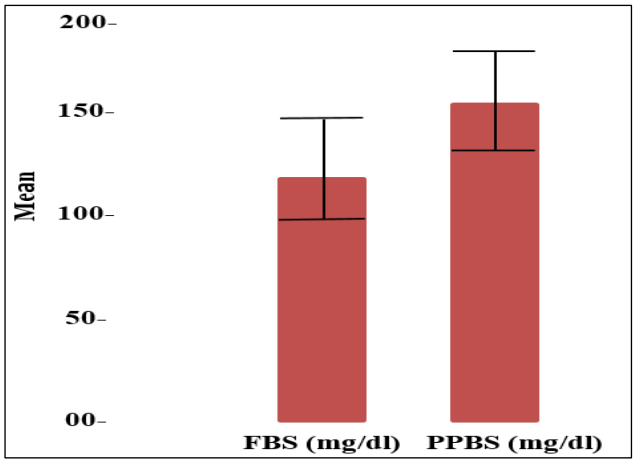

Figure 1: Blood glucose levels in study subjects.

Table 2: Clinical variables in study subjects.

Variables		Frequency n=67	%
HbA1c	</=6.5	19	28.4
	>6.5	48	71.6
Duration of diabetes (yrs)	</=10	47	70.1
	>10	20	29.9
BMI (kg/m^2)	Underweight	3	4.5
	Normal	47	70.1
	Overweight	15	22.4
	Obese	2	3.0
Pulmonary function	Normal	57	85.1
	Restrictive	10	14.9
	Obstructive	0	0
	Mixed	0	0

Table 3: Comparison of parameters between subjects with normal and restrictive.

Parameters	Pulmonary function	N	Mean	SD	t	P value
Age (yrs)	Normal	57	49.63	8.19	-2.71	0.01*
	Restrictive	10	54.30	4.24		
BMI	Normal	57	23.48	2.99	-0.66	0.513
	Restrictive	10	24.12	1.46		
HbA1c (g%)	Normal	57	7.07	0.78	-0.79	0.43
	Restrictive	10	7.28	0.77		
Duration of diabetes (yrs)	Normal	57	7.37	5.05	-3.77	<0.01**
	Restrictive	10	13.80	4.49		
FBS (mg/dl)	Normal	57	115.23	18.22	0.65	0.52
	Restrictive	10	112.20	12.56		
PPBS (mg/dL)	Normal	57	152.18	24.81	0.47	0.68
	Restrictive	10	148.30	17.54		

There was no significant difference found between two groups regarding rest of the parameters (BMI, HbA1c, FBS and PPBS) (Table 3). FVC (L) P having mild downstream (r= -0.247, P=0.044*) with age and duration of disease (r= -0.247, P=0.044*). FVC (L)%P and FVC (L)% showing mild correlation (r=-0.400, P=0.001** and r=-0.393, P=0.001** respectively) with duration of disease. FEV1 (L) P and FEV1/FVC%P showing mild downstream (r= -0.260, P=0.033* and r=-0.320, P=0.008*respectively) with duration of disease (Table 4).

DISCUSSION

Diabetes mellitus is a chronic disease associated with various micro and macrovascular complications. Present study finding showed that majority of the subjects were male, belonged to the sixth decade of life with a mean age of 50.3±7.14 years, having normal BMI and pulmonary function was normal. Pulmonary function was found to be restrictive in 14.9% subjects. Study findings show that diabetes mellitus was more common in old age group (>50years of age) and in male population (>45%)[12,14-16]

Table 4: Correlation analysis of pulmonary function test with various parameters.

Pulmonary function test	Parameter	Pearson's r	P-value	Significance/interpretation
FVC (L) P	Age	-0.247	0.044*	Mild downstream
	BMI	0.141	0.25	No correlation
	HbA1C	0.032	0.79	No correlation
	Duration of Disease	-0.247	0.044*	Mild downstream
FVC (L)%P	Age	-0.208	0.09	No correlation
	BMI	0.053	0.67	No correlation
	HbA1C	-0.068	0.58	No correlation
	Duration of Disease	-0.400	<0.01**	Mild correlation
FEV1 (L) P	Age	-0.238	0.053	No correlation
	BMI	0.108	0.383	No correlation
	HbA1C	0.025	0.838	No correlation
	Duration of Disease	-0.260	0.033*	Mild downstream
FVC (L)%	Age	-0.208	0.091	No correlation
	BMI	0.056	0.651	No correlation
	HbA1C	-0.025	0.843	No correlation
	Duration of Disease	-0.393	<0.01**	Mild correlation
FEV1/FVC%P	Age	-0.192	0.119	No correlation
	BMI	-0.087	0.484	No correlation
	HbA1C	-0.046	0.709	No correlation
	Duration of Disease	-0.320	<0.01*	Mild downstream
FEV1/FVC%	Age	-0.187	0.131	No correlation
	BMI	-0.026	0.836	No correlation
	HbA1C	0.035	0.777	No correlation
	Duration of Disease	-0.087	0.483	No correlation

The mean FBS was 114.8±17.5mg/dl while mean PPBS was 151.6±23.8mg/dl. Majority of the subjects were having an abnormally high level of HbA1c and they had </=10years duration of DM. Few studies has concluded that the HbA1c level in diabetic subjects remains towards the higher side (>6.5). The incidence of diabetes was increasing and most of the subjects having a diabetes duration of </=10years.[16-18]

Pulmonary function was normal in most of the subjects and it was restrictive in 14.9% subjects. No subjects with obstructive PFT pattern were present in this study. In a prospective study by Davis W et al, mean percentage-predicted values of each spirometry measure were decreased 10% in the whole cohort at baseline and absolute measures continued to decline at an annual rate of 68, 71 and 84ml/year and 17l/min for FVC, FEV1, VC and PEF, respectively.[15] Davis W et al, reported that the means of all spirometry measures were reduced by >9.5%.[19] Yeh HC et al, reported adults with diabetes had significantly lower predicted FVC and predicted FEV1 than those without diabetes.[20] Benbassat C et al, however, reported no such significant changes in pulmonary function tests in type 2 DM subjects.[16]

Older age and longer duration of diabetes were found to be significantly associated with deranged pulmonary function tests in study subjects with diabetes mellitus. No such association of PFT was detected with BMI, HbA1c, fasting or postprandial blood sugar. Davis W et al, in their study reported similar findings stating after controlling for smoking, age and gender in a linear regression model, HbA1c was not associated with any measure of lung function but diabetes duration was significantly associated with FEV1% pred and PEF% pred and had borderline associations with FVC% pred and VC% pred.[19] Shah SH et al and Yeh HC et al, also concluded that the declining lung function to be in

inverse relation to diabetes severity and pulmonary function test parameters were significantly reduced except FEV1/FVC in patients of type 2 DM.[17,20] Meta-analysis by Borst BB et al, showed that DM is associated with an impaired pulmonary function in a restrictive pattern.[13] Patients with type 2 DM were at increased risk of several pulmonary conditions like-asthma, Chronic Obstructive Pulmonary Disease (COPD), fibrosis and pneumonia. A study by Sinha et al, and Benbassat et al, failed to observe a significant difference in any of the PFT parameter except for DLCO and reported a lack of association.[16,21]

Normal lung mechanics and gas exchange are influenced by the integrity of the pulmonary connective tissue and microvasculature. Acceleration of aging process in connective tissue cross-links and presence of nonenzymatic glycosylation and modification of alveolar surfactant action causes a reduction in PFTs. There have been reports of histopathological changes in the diabetic patients.[21] Diabetic microangiopathy might be existing in the pulmonary vascular bed. Moreover, reduced pulmonary capillary blood volume was found, favoring the evidence of microangiopathy. This could lead to a redistribution of the pulmonary circulation resulting in well-ventilated areas to become under-perfused.[22] The thorax and lungs are rich in collagen and elastin. Stiffening of thorax and lung parenchyma can occur because of nonenzymatic glycosylation of these structural compounds. This may lead to the restrictive pattern. In this study, restrictive pattern in DM patients strongly suggests this mechanism of derangement in PFT. Duration of diabetes was significantly associated with the restrictive pattern in this study is further strengthens this hypothesis. With increasing duration of disease, the more exposure of the tissues and microvasculature to the hyperglycemic environment is expected and thus nonenzymatic glycation will also increase.

However, there are certain studies showing no correlations between HbA1c and PFTs. They argued that HbA1c levels are indicators of glycemic control for a short period of 1-2months, it was not adequate to conclude that the plasma glucose level was not related to decreased PFTs. While some studies have shown that the decline in PFTs was negatively correlated with HbA1c.[16,23,24]

In present study, FVC (L) P showed mild downstream correlation with age and duration of diabetes. No correlation with BMI and the HbA1c level was observed. Correlation of FVC (L) %P was found to be mild downstream with duration of disease only. FEV1 (L) P and FEV1 (L) %P also showed similarly mild downstream correlation with duration of disease only and both failed to show correlation with any other parameters. FEV1/FVC% P also showed mild downstream correlation with duration of disease. So, in a nutshell, most of the PFT parameters showed Mild downstream correlation with duration of disease. None of the parameters were found to show correlation with HbA1c. Marvisi M et al, found that both HbA1c and age of subjects showed no correlation with deranged PFT (DLCO). However, microangiopathy i.e. diabetic nephropathy and diabetic retinopathy both showed strong and moderate correlation respectively. This duration and control dependent complications can be considered surrogate markers for the duration of disease and long-term glycemic control and thus it can be extrapolated that the PFT is related to the duration of disease and long-term glycemic control.[24] Similarly, Ljubić S et al revealed that the age, duration of diabetes and complication parameters were found to be significant predictors of DLCO/VA. However, proteinuria was the only significant independent predictor of DLCO/VA.[25] There are certain studies showing no correlation between HbA1c and PFTs which support this finding. It might be due to that HbA1c levels are indicators of glycemic control for a short period of 1-2months, it was not adequate to conclude that the plasma glucose level was not related to decreased PFTs.

CONCLUSION

Diabetes mellitus (DM) is one of the costliest chronic diseases of this time and is a condition that is increasing in epidemic proportions throughout the world. Type 2 diabetes mellitus is associated with the development of microvascular and macrovascular complications. Chronic hyperglycemia in diabetes may lead to diabetes-associated systemic inflammation which results in airway and lung damage. Diabetes was more common in the sixth decade of life with slight male preponderance. The most common PFT derangement pattern in diabetic subjects is a restrictive pattern and having a significantly longer duration of a diabetic. The short-term indicators of glycemic controls were not significantly associated with a restrictive pattern of PFT. Despite the best effort, there are limitations of present study, which includes small sample size, author have not taken general population, and lack of a control group. these limitations can be overcome in the future studies. Published work from this research may help educate the healthcare holders with evidence-based literature on the prevalence of chronic pulmonary complications and the nature of the complications in T2DM. This may influence behavior changes and consequently improve the rates of pulmonary disease morbidity and mortality in patients with T2DM.

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