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ORIGINAL ARTICLE

Association of Glycaemic Status (Hba_1c) with FEV_1 and FEV_1/ FVC Ratio in COPD Patients with Type 2 Diabetes Mellitus

Prottush Kumar Mondal[1], Md. Sayedul Islam[2], Md. Khairul Anam[3], Nihar Ranjan Saha[3], SK. Shahinur Hossain[3], Manoranjan Roy[4], Md. Habibur Rahman[5], Chitta Ranjan Paul[5], Goutam Sen[5]

Abstract

Background: *Diabetes mellitus (DM) is an important and common comorbid condition associated with chronic obstructive pulmonary disease (COPD). Diabetes damages major organ systems through disrupted glycemic control and increased inflammation. Reduced pulmonary function has been observed in patients with type 2 diabetes. This functional impairment has been shown primarily through cross-sectional associations between glycemic status (HbA_1c) with FEV_1 and FEV_1/FVC ratio.*

Materials & Methods: *This Cross sectional observational study was conducted in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH) from December 2019 to March 2021. Eighty Two diagnosed cases of COPD with type 2 DM who were treated in NIDCH were enrolled purposefully in this study.*

Results: *Sixty two percent (62.2%) patients had moderate obstruction (FEV_1 79-50 percent) with mean FEV_1 was 56.3±13.1 percent predicted. More than three fourth (76.8%) patients had FEV_1/FVC ratio 60-69 percent with mean FEV_1/FVC ratio was 63.3±4.7 percent predicted. Mean FEV_1 and FEV_1/FVC ratio was significantly lower in uncontrolled glycaemic status (HbA_1C) (p=0.001). In multivariate regression analysis, uncontrolled HbA_1C was found to be an independent predictor for low FEV_1 (<50%).*

Conclusion: *This study concluded that FEV_1 and FEV_1/FVC ratio were significantly lower in uncontrolled glycaemia than controlled glycemic group of COPD patients with type 2 DM. Uncontrolled HbA_1C was found to be independent predictor for low FEV_1 (<50%).*

Keyword: Hemoglobin A_1C (HbA_1C), Forced expiratory volume in one second (FEV_1), Forced vital capacity (FVC), Chronic obstructive pulmonary disease (COPD), Type 2 DM.

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1. Registrar, Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka.
2. Director & Professor, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
3. Associate Professor, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
4. Assistant Professor, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
5. Medical Officer, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.

Correspondence to: Dr. Prottush Kumar Mondal, MBBS, MD (Pulmonology), Registrar, Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka. E-mail: prottushkumarmondal17@gmail.com, Mobile: 01712064318.

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Introduction:

Chronic obstructive pulmonary disease can be described by air flow limitation and chronic inflammatory disorder of lungs which is progressive and partially reversible through treatment and which occurs because of exposure of noxious particles and gases for a long term.[1] When chronic cough and sputum from airways for at least three months in each of two successive years without any other causes of chronic cough; associated with irreversible airflow limitation; then the group of chronic bronchitis and emphysema together defined as chronic obstructive pulmonary disease.[2] It has been associated with various systemic and co-morbid conditions like ishchaemic heart disease, type 2 diabetes, hypertension, osteoporosis, malnutrition, skeletal muscle dysfunction, endocrine disorders, lung cancer and anxiety.[1]

COPD determined as one of the main causes of mortality worldwide. In 2005, globally, COPD was responsible for 5% of all deaths.[3] It has been predicted to become the third leading cause of death worldwide by 2030.[4]

According to World Health Organization (WHO), sixty-five million people suffer from moderate to severe form of chronic obstructive pulmonary disease.

Diabetes mellitus is selected as a chronic condition also and increasing rate of diabetes leads to affect around 600 million people by 2035.[5] Progression of COPD can be increased by type 2 DM which causes COPD-related mortality. Other studies showed that, patients of COPD gained a protective effect from the Diabetes-associated adiposity which can reduce the death of individuals having COPD.[5]

Some studies have showed that, in COPD patient, there are impact on both lung function and quality of life. Many other studies describe that, DM is associated with impaired pulmonary function. Other studies suggest that there are no association between DM and lung function.[4]

Inhaled corticosteroid which is usually prescribed in case of patient of COPD was also related with increased incidence of type 2 DM.[6]

Development of COPD can be caused by Diabetic patients as well as COPD patients are also at risk of developing diabetes mellitus because of sedentary life, smoking, obesity, oxidative stress, increased inflammatory condition and corticosteroid therapy.[4]

90% of diabetes cases represent type 2 DM which results commonly from adiposity and sedentary lifestyle, having genetic predisposition.[7]

Combination of insulin resistance and non-functioning pancreatic beta cells that causes failure of control of blood glucose level of an individual are the characteristic features of type 2 DM. Increased incidence and prevalence of diabetes mellitus specifically in Asians are being alarming day by day.[8]

Respiratory system is affected by hyperglycemia through the induction of oxidative stress, systemic inflammation, hypoxemia, altered gas exchange and structural changes of lung tissue.[5] Diabetes and prior to development of diabetes have associated with obstruction on spirometry.[4] Airflow limitation and reduced lung volume are chronic complications of type 2 DM. Lower forced expiratory volume in 1s (FEV_1) and forced vital capacity (FVC) are the features of diabetic patients also.[5]

In case of diabetic patient, four sources are selected as the origins of lung function impairment: such as (a) non-enzymatic glycosylation of lung elastin and collagen reduces the elasticity of the lung, (b) Reduction of blood volume of pulmonary capillary and diffusing capacity by thickening of alveolar epithelial basal lamina and microvascular changes in pulmonary capillary beds, (c) Reduction of muscle tone of diaphragm can be created by autonomic neuropathic lesion of the phrenic nerves, and (d) Hyperglycemia induced increased bacterial colonization is responsible for frequent acute exacerbations of COPD.[9]

To address these issues, this study was conducted to assess the lung function among the individuals who have both COPD and type 2 Diabetes Mellitus and explore the relationship between lung function and glycaemic control of patients with COPD.

Material and methods:

This cross-sectional observational study was carried out in the outpatient department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka over a period December 2019 to March 2021.

The sample of the study was selected using consecutive sampling technique. From the attendees of outpatient department (OPD), a group of patients with COPD and type 2 DM was selected using a non-probability consecutive sampling technique. The consecutive sampling technique provides the opportunity to choose eligible

participants until the desired sample size were reached. Subjects with exacerbation, asthma, pneumonia, pulmonary TB, bronchiectasis, DPLD, bronchial carcinoma and cardiac disease were excluded in this study.

Glycaemic control was defined according to the HbA_1C target of <7.0% as recommended by American Diabetes Association.[10]

Statistical Package for Social Science (SPSS) version 23 for windows was used to analyze the data. Statistical analysis was done by unpaired 't' test and multiple regression analysis as applicable. P values <0.05 was considered as statistically significant.

Results:

The association of glycaemic status (HbA1c) with FEV_1 and FEV_1/ FVC ratio in COPD patients with type-2 diabetes mellitus. This cross-sectional observational study was carried out in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. A total of 82 patients with stable COPD with type 2 diabetes mellitus were included in this study, who fulfilled the inclusion and exclusion criteria. The findings obtained from data analysis are presented below.

Majority 36(43.9%) patients belonged to age 61-70 years. The mean age was found 59.2±6.5 years with range from 45 to 69 years. Majority 78(95.1%) patients were male with male-female ratio 19.5:1. Thirty five 35(42.7%) were businessman. The mean BMI was found 25.1±2.8 kg/m^2 with range from 20.6 to 30.6 kg/m^2 [Table-I]. 68(82.9%) patients were found HbA_1C e"7 percent. The mean HbA_1C was found 8.2±1.4 percent with range from 6.2 to 12.9 percent [Table-II].

Study shows that 51(62.2%) patients had moderate FEV_1 (79-50 percent). The mean FEV_1 was found 56.3±13.1 percent with range from 27 to 88 percent. More than three fourth (76.8%) patients had FEV_1/ FVC ratio 60-69%. The mean FEV_1/FVC ratio was 63.3±4.7 percent with range from 53 to 69 percent [Table-III].

In this study 43(63.2%) patients were found FEV_1 level 79-50 percent in uncontrolled glycaemic group and 8(57.1%) in controlled glycaemic group. The mean FEV_1 was found 54.1±11.6 percent in uncontrolled glycaemic group and 66.9±14.9 percent in controlled glycaemic group. So, it reveals that the mean FEV_1 (%)was significantly lower in uncontrolled glycaemic group than controlled glycaemic group and the difference was statistically significant (p<0.05) between two groups [Table-4]. Similarly 49(72.1%) patients had FEV_1/ FVC ratio 60-69% in uncontrolled glycaemic group and 14(100.0%) in controlled glycaemic group. The mean FEV_1/FVC ratio was found 62.4±4.8 percent in uncontrolled glycaemic group and 67.3±1.7 percent in controlled glycaemic group. So, here it has been shown that mean FEV_1/FVC ratio (%) is significantly lower in uncontrolled than controlled glycaemic group and the difference was statistically significant (p<0.05) between two groups [Table-V].

In multivariate analysis, uncontrolled HbA_1C was found to be an independent predictor for lowFEV_1 as here p value is low (p<0.05). However, age, male, tobacco use, hypertension and obesity were not found to be independent predictors for lowFEV_1 as in every condition p value is high (p>0.05) [Table-VI]. Multivariate analysis also reveals age, male, tobacco use, hypertension, obesity and uncontrolled HbA_1C were not found to be independent predictors for lower FEV_1/FVC ratio (<60%) because in every conditions p value was high (p>0.05) [Table-VII].

Table-I

Patient demography (n=82)

Variables	Frequency	Percentage
Age (years)		
41-50	13	15.9
51-60	33	40.2
61-70	36	43.9
71-80	0	0.0
Mean±SD	59.2±6.5	
Range (min-max)	45.0-69.0	
Sex		
Male	78	95.1
Female	4	4.9
Occupational status		
Businessman	35	42.7
Service holder	20	24.4
Cultivator	19	23.2
House wife	4	4.9
Shopkeeper	2	2.4
Cook	2	2.4
BMI (kg/m^2)		
<18.5	0	0.0
18.5-24.9	52	63.4
25.0-29.9	23	28.0
≥30.0	7	8.5
Mean±SD	25.1±2.8	
Range (min-max)	20.6-30.6	

Table-II

Distribution of the patients according to glycaemic status based on HbA$_1$C (n=82)

HbA$_1$C (%)	Frequency	Percentage
<7.0 (Controlled)	14	17.1
≥7.0(Uncontrolled)	68	82.9
Mean±SD	8.2±1.4	
Range (min-max)	6.2-12.9	

Spirometric variations of study population (n=82)

Table-III

Spirometric variables of study population (n=82)

FEV$_1$ (%)	Frequency	Percentage
<30 (Very severe)	2	2.4
49-30 (Severe)	22	26.8
79-50 (Moderate)	51	62.2
≥80 (Mild)	7	8.5
Mean±SD	56.3±13.1	
Range (min-max)	27.0-88.0	
FEV$_1$/FVC ratio (%)		
50-59	19	23.2
60-69	63	76.8
Mean±SD	63.3±4.7	
Range (min-max)	53.0-69.0	

Table-IV

Association between FEV$_1$ with glycaemic status of study population (n=82)

FEV$_1$ (%)	Glycaemic status (HbA$_1$C)				t value	P value
	Uncontrolled(n=68)		Controlled(n=14)			
	n	%	n	%		
<30 (Very severe)	2	2.9	0	0.0		
49-30 (Severe)	20	29.4	2	14.3		
79-50 (Moderate)	43	63.2	8	57.1		
≥80 (Mild)	3	4.4	4	28.6		
Mean±SD	54.1±11.6		66.9±14.9		3.57	0.001^s
Range (min-max)	27.0-82.0		40.0-88.0			

s= significant

P value reached from unpaired t-test

Table-V

Association between FEV_1/FVC ratio with glycaemic status of study population (n=82)

FEV_1/FVC ratio (%)	Glycaemic status (HbA_1C)				t value	P value
	Uncontrolled(n=68)		Controlled(n=14)			
	n	%	n	%		
50-59	19	27.9	0	0.0		
60-69	49	72.1	14	100.0		
Mean±SD	62.4±4.8		67.3±1.7		3.75	0.001[s]
Range (min-max)	53.0-69.0		64.0-69.0			

s= significant

P value reached from unpaired t-test

Table-VI

Multivariable Regression Analysis for low FEV_1 (<50%)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (≥61 years)	0.501	0.172	1.459	0.205[ns]
Male	2.982	0.431	84.407	0.980[ns]
Tobacco use	1.188	0.197	6.854	0.864[ns]
Hypertension	1.905	0.644	5.635	0.244[ns]
Obesity	0.231	0.026	2.424	0.249[ns]
Uncontrolled HbA_1C	2.668	1.129	6.287	0.023[s]

s= significant, ns= not significant; OR=Odds Ratio

p value reached from multivariate analysis by binary logistic regression analysis

Table-VII

Multivariable Regression Analysis for lower FEV_1/FVC ratio (<60%)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (≥61 years)	1.788	0.410	5.968	0.309[ns]
Male	2.112	0.151	88.340	0.989[ns]
Tobacco use	1.174	0.218	8.287	0.738[ns]
Hypertension	0.752	0.368	3.993	0.752[ns]
Obesity	0.272	0.027	2.698	0.266[ns]
Uncontrolled HbA_1C	0.186	0.082	1.097	0.062[ns]

ns= not significant; OR=Odds Ratio

p value reached from multivariate analysis by binary logistic regression analysis

Discussion:

This cross sectional observational study was carried out with an aim to assess the association of glycaemic status (HbA_1c) with FEV_1 and FEV_1/FVC ratio in COPD patients with type 2 DM attending in outpatient department of NIDCH. Out of 82 patients of COPD with type 2 diabetes mellitus who fulfilled the inclusion and exclusion criteria during the period from December 2019 to March 2021 were included in this study.

In this study it was observed that majority 36(43.9%) patients belonged to age 61-70 years. The mean age was found 59.2±6.5 years with range from 45 to 69 years. Almost similar study conducted by Ajit et al.[3] where they found the mean age among study participants was 58.4±11.6 years. Mekov et

al.[4] reported mean age of patients was 65.1±9.9 years. Another study conducted by Adiody et al.[1] where they observed maximum patients were in the age group of 61-70 years showing that COPD commonly affects the elderly population.

Here it has been found majority 78(95.1%) patients were males and 4(4.9%) were females. Male-female ratio was 19.5:1. Almost similar study documented by Ajit et al.[3] where they showed out of 412 patients, 328 (79.6%) were males and 84 (21.6%) females with male-female ratio 3.9:1. Nemagouda[11] described out of 52 patients, males were 30(58%) and females were 22(42%). Mekov et al.[4] also consisted that 71.1% were males, 28.9% were females.

This study revealed almost two third (63.4%) patients were normal body mass index (BMI). The mean BMI was found 25.1±2.8 kg/m^2 with range from 20.6 to 30.6 kg/m^2. In a study done by Ajit et al.[3] where they observed mean body mass index of the participants was 23.47±3.7 kg/m^2. Nemagouda[11] also found the mean BMI was 23±2.4 kg/m^2.

Regarding glycaemic status based on HbA_1C in this study we have found 68(82.9%) patients were found HbA_1C ≥7 percent. The mean HbA_1C was found 8.2±1.4 percent with range from 6.2 to 12.9 percent. In Bangladeshi study conducted by Ali et al.[12] where they observed mean HbA_1C was found 6.48 percent in type 2 DM patients with diabetic duration 5-10 years and 7.21 percent in diabetic duration 10-20 years. Adiody et al.[1] reported mean HbA_1C was found 7.9±1.89 percent. Lecube et al.[13] described mean HbA_1C was found 7.5±1.4 percent. Another study conducted by Nemagouda[11] where they showed the mean HbA_1C was 8.8±1.7 percent.

Among the total 82 study patients 7(8.5%) had mild FEV_1 (≥80 percent), 51(62.2%) patients had moderate FEV_1 (79-50 percent) followed by 22(26.8%) had severe FEV_1 (49-30 percent), and only two (2.4%) had very severe FEV_1 (<30 percent). The mean FEV_1 was 56.3±13.1 percent with range from 27 to 88 percent. In a study of Ajit et al.[3] showed that the prevalence in mild, moderate, severe, and very severe COPD was 14.73%, 18.94%, 36.84% and 29.47%, respectively. Mekov et al.[4] reported that the mean FEV_1 was 55.34±19.5 percent. Lecube et al.[13] consisted the mean FEV_1 was found 88.4±19.7 percent.

Regarding association between FEV_1 with glycaemic status in this study it has been revealed 43(63.2%) patients were found FEV_1 level 79-50 percent in uncontrolled glycaemic group and 8(57.1%) in controlled glycaemic group. The mean FEV_1 was found 54.1±11.6 percent in uncontrolled glycaemic group and 66.9±14.9 percent in controlled glycaemic group. FEV_1 was significantly higher in controlled group than uncontrolled group ($p<0.05$). In the study done by Ajit et al.[3] where they showed that there was a severe decline in lung function (mean FEV_1 45.92±4.22) in people with diabetes as compared to non-diabetics (56.64±3.58) and it was found to be statistically significant ($P = 0.001$). Tanni et al.[14] consisted that the mean percentage of predicted value of FVC and FEV_1 were significantly lower in T2DM than those of control ($p<0.001$). Ali et al.[12] described the mean percentage of predicted values of FVC and FEV_1 in DM group was significantly ($p<0.001$) lower than those of control group. Nemagouda[11] reported the FEV_1, FVC & FEV_1/FVC had statistically significant difference with respect to BMI & HbA1c ($p <0.05$). The severity related to the duration & poor glycaemic control of type 2 diabetes mellitus. Dennis et al.[15] and McKeever et al.[16] in their studies have reported that diabetics with inadequate glucose control have a lower pulmonary function as compared to those with adequate control.

Regarding association between FEV_1/FVC ratio with glycaemic status in this study we have found 49(72.1%) patients had FEV_1/FVC ratio 60-69 percent in uncontrolled glycaemic group and 14(100.0%) in controlled glycaemic group. The mean FEV_1/FVC ratio was found 62.4±4.8 percent in uncontrolled glycaemic group and 67.3±1.7 percent in controlled glycaemic group. FEV_1/FVC ratio was significantly lower in uncontrolled group than controlled group ($p<0.05$). Adiody et al.[1] had observed their study lung function in terms of FEV_1, FVC, FEV_1/FVC, FEF 25-75 were the least in COPD with DM group than DM group. Ali et al.[12] documented that the mean percentage of predicted values of FEV_1/FVC (%) were significantly higher ($p<0.001$) in diabetic duration 10-20 years compared to 5-10 years. El Habashy et al.[17] showed that there was a significant decrease in pulmonary function tests among diabetic patients (FEV_1, FEV_1/FVC%, forced expiratory flow –25%–75%, maximal

voluntary ventilation, and PEF) compared with healthy controls and further proved that decline was exaggerated in poorly controlled DM. Tanni et al.[14] consisted that the difference in FEV_1/FVC between the groups was not significant. Several studies results showed significant lower values of all lung function parameters except FEV_1/FVC ratio strongly suggests impaired lung function in T2DM.[18-20]

In multivariable regression analysis, uncontrolled HbA_1C was found to be independent predictor for air way obstruction low (FEV_1 <50%). However, age, male, tobacco use, hypertension and obesity were not found to be independent predictors for low FEV_1. Another multivariate regression analysis was found age, male, tobacco use, hypertension, obesity and uncontrolled HbA_1C were not found to be independent predictors for lower FEV_1/FVC ratio (<60%). Rana et al.[21] observed that COPD patients had a multivariate relative risk of 1.38 (95% confidence interval [CI]: 1.14–1.67) for new onset type 2 DM. Mekov et al.[4] reported linear regression analysis shows that HbA_1C is a risk factor for lower FVC (R = 0.166, r2 = 0.027, p = 0.041, B = -3.116, 95% CI -6.111-0.122). Peng et al.[22] consisted linear associations of FVC% and FEV1% with risk of T2DM were found (Pnon-linearity > 0.05). Another study conducted by Baba et al.[23] documented that logistic regression analysis revealed that age (>60 years), HbA_1c levels (>5.6%), current smoking, and former smoking were significantly associated with a FEV_1/FVC <70%.

From above discussion in brief, it has been shown that out of 82 study patients of COPD with type 2 diabetes mellitus majority of the study patients were in uncontrolled glycaemic group. Mean FEV_1 (%) & FEV_1/FVC ratio (%) were significantly lower in patients of uncontrolled glycaemia than controlled glycaemic group. There was significant association of FEV_1 (%) & FEV_1/FVC ratio (%) with glycaemic status.

Conclusion:

This study revealed that there was significant association between HbA_1C with FEV_1 and FEV_1/FVC ratio in COPD patients with type-2 DM. Strict glycemic control is an important issue in those patients as uncontrolled glycaemia is associated with low FEV_1 and low FEV_1/FVC ratio.

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