Original Research Article

Burden of Type 2 Diabetes Mellitus among Chronic Obstructive Pulmonary Disease Patients: Challenge of dual Co-Morbidities among Indians?

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Abstract

Introduction: Non Communicable diseases (NCDs) like chronic respiratory diseases, stroke, cardiovascular diseases, metabolic disorders like diabetes and obesity are burden on the global health. Chronic obstructive pulmonary disease (COPD) is projected to the third leading cause of death in world by 2030. Chronic obstructive pulmonary disease can lead to diabetes mellitus (DM) and vice versa. **Objective:** To find out the prevalence of type 2 diabetes mellitus (T2DM) among COPD patients. **Materials and Methods:** Total 369 study participants were included in the study. Estimation of Fasting Plasma glucose (FPG), Post Prandial Plasma Glucose and Gylcated Hemoglobin (HbA1C) and Anthropometric measurements were done as per WHO guidelines. Type 2 Diabetes Mellitus was diagnosed as per American Diabetes Association (ADA). COPD was diagnosed and classified as per © 2020, Global Initiative for Obstructive Lung Diseases (GOLD). **Result**: Prevalence of T2DM was found to be 39.6%, 20.3% were known cases of T2DM and 19.2% were newly diagnosed. Increasing age, female gender, urban residence, longer duration of COPD, high BMI and smoking were found to be significant risk factors for T2DM among COPD patients. Presence of T2DM was associated with significantly more severe COPD cases. **Conclusion:** High prevalence of T2DM was found among COPD patients. More frequent screening of T2DM and good control of T2DM should be done because about 1/5th of the COPD patients had newly diagnosed T2DM and presence of T2DM significantly resulted in more severe disease.

Keywords: T2DM, COPD, COPD GRADING, GOLD Criteria

Introduction

Non Communicable diseases (NCDs) like chronic respiratory diseases, stroke, cardiovascular diseases, metabolic disorders like diabetes and obesity are burden on the global health[1-2]. Chronic obstructive pulmonary disease (COPD) is projected to the third leading cause of death in world by 2030[3]. COPD can substantially increase economic and co morbidity burden[4-5]. COPD can be clinically characterized by persistent cough and shortness of breath, the symptoms worsens with disease progression. All patients' shows reduced expiratory flow rates on pulmonary function tests[6]. COPD is frequently associated with co morbidities like cardiovascular diseases, metabolic syndrome, skeletal and muscular disorders, etc[7-8]. These co morbidities affect the exacerbation frequency and prognosis of the COPD[6,9]. Chronic respiratory disorders and diabetes are common among elderly people[10-11]. Chronic obstructive pulmonary disease can lead to diabetes mellitus (DM) and vice versa[12].

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Since, initially both COPD and Diabetes mellitus presents as low grade inflammation, few authors considers COPD as a unique risk factor for Type 2 diabetes mellitus (T2DM)[13-14]. Markers of systemic inflammation like C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) has an important role in the onset of insulin resistance as well as in the progression of COPD[15]. Diabetes Mellitus can be defined as a "chronic metabolic disorder resulting from either insulin resistance or relative or absolute insulin deficiency"[16]. India is home of about 73 million diabetes patients which is expected to be 134 million by 2045[17]. Important modifiable risk factors for T2DM are unhealthy diet, physical inactivity, obesity, smoking, harmful use of alcohol and stress[18-19]. Although there is debate on the extent of impairment, Diabetes Mellitus is indeed associated with statistically significant impairment of pulmonary function[12,20-21]. Since both COPD and DM have high prevalence among aged population, this study aims to find out the prevalence of type 2 diabetes mellitus (T2DM) among COPD patients.

Materials and methods

An Institution based, observational, Cross-Sectional study was conducted at IQ City Medical College, Durgapur from July 2019 to Dec 2019. This study was ethically cleared by Institutional Ethics

Committee (IEC) [Ref. No. IQMCIEC/LTR/18/04/ 23 (11)] of IQ City Medical College. Data were collected after getting written informed consent from all the study participants.

Total 369 study participants were included in the study. Sample size was calculated using standard World Health Organization (WHO) guideline[22] using formula $4PD/d^2$. Considering the prevalence (P) of vitamin deficiency 23.0%[23], Q= (1-P), absolute precision of 5 with 95% confidence interval, Allowable error 20% of P, and 10.0% non-response rate minimum sample size came to be 369. Systematic random sampling was used to select the study participants. Every month, approximately 700 COPD patients attend the Respiratory OPD of IQ City. The estimated total COPD number for study duration was about 4200. Sample interval of 12 was obtained by dividing estimated OPD attendance with sample size. Every 12th patient was included in the study till desired sample size of 369 study participants was reached. A predesigned, pretested semi structured schedule was used to collect socio demographic data. 3 ml of venous blood samples were collected from antecubital vein using all aseptic measures. Estimation of Fasting Plasma glucose (FPG), Post Prandial Plasma Glucose and Gylcated Hemoglobin (HbA1C) was done as per WHO guidelines[24]. Type 2 Diabetes Mellitus was diagnosed as per American Diabetes Association (ADA)[25-26]. Anthropometric measurements were taken as per standard WHO guidelines[27]. COPD was diagnosed and classified as per © 2020, Global Initiative for Obstructive Lung Diseases (GOLD)[28]. As per the GOLD guidelines, main criterion for COPD diagnosis is a FEV1/FVC ratio <70%. COPD severity was classified as GOLD 1 (mild), GOLD 2 (Moderate), GOLD 3 (Severe) and GOLD 4 (Very Severe) if FEV1 was ≥ 80% predicted, 50% to <80% of predicted, 30% to <50% of predicted and <30% of predicted respectively[28].

Statistical Analysis

All the data were codified and entered in MS Excel spread sheet. Data were analyzed using SPSS software, Version 20.0 (SPSS Inc, Chicago, IL, USA). "Chi-Square test" was used to show association of categorical variables. One way ANOVA with tukeys post hoc test was done to show association between Mean HbA1C level and COPD severity. P-value ≤0.05 was considered as statistically significant.

Results

Data from 369 study participants were analyzed. Mean age of the study population was 62.89±10.75 years. 31.4% of the study participants were ≥71 years of age followed by 27.1%, 26.1% and 15.4% were in age group of 61-70 years age group, 51- 60 years age group and 41-50 years of age group respectively (Table-1). 74.8% of study population was Male and 25.2% were female. 51.2% of study participants were from rural area and 48.8% was from urban area. Smoking history was found in 68.6% of study participants. While Mean BMI of the study participants was 25.62±4.57 kg/m^2, 58.8% of study participants had BMI ≥25.0 kg/m^2 and 41.2% had BMI 18.5-24.99 kg/m^2 (Table-1). Mean duration of COPD was 4.58±3.27 Years, 70.7% of the study participants had COPD for < 5years duration and 29.3% of them had COPD for ≥ 5 years. 29.3% of study population had severe COPD followed by 27.4%, 24.9%and 18.4% had moderate, very severe and mild COPD respectively (Table-1). Prevalence of T2DM was found to be 39.6%, 20.3% were known cases of T2DM and 19.2% were newly diagnosed (Table-1).

Table-1: Clinico-Social (CS) Characteristics of Study Population, n=369

Clinico-Social characteristics	n(%)
Age group	
41-50 years	57 (15.4)
51-60yrs	96 (26.1)
61-70 yrs	100 (27.1)
≥71 years	116 (31.4)
Sex	
Male	276 (74.8)
Female	93 (25.2)
Residence	
Urban	180 (48.8)
Rural	189 (51.2)
Smoking	
Yes	253 (68.6)
No	116 (31.4)
BMI (Kg/m^2)	
Normal (18.5-24.99)	152 (41.2)
Overweight/Obese (≥23.00)	217 (58.8)
Duration of COPD	
<5 Years	261 (70.7)
≥ 5 Years	108 (29.3)
Severity of COPD	
GOLD 1 (Mild)	68 (18.4)
Gold 2 (Moderate)	101 (27.4)
Gold 3 (Severe)	108 (29.3)
Gold 4 (Very Severe)	92 (24.9)
T2DM* Diagnosis	
Known T2DM	75 (20.3)
Newly Diagnosed T2DM	71 (19.2)
No T2DM	223 (60.5)
Prevalence of T2DM	
Yes	146 (39.6)
No	223 (60.4)

***T2DM- Type 2 Diabetes Mellitus**

67.2% of participants older than ≥71 years of age had T2DM as compared to 35.0%, 21.9% and 21.1% in the age group of 61-70 years, 51-60 years and 41-50 years respectively. Increasing age group was found to be a significant risk factor for T2DM among COPD patients (Table-2).

Table-2: Chi Square test Showing association between Clinico-social determinants and T2DM (n=369)

C-S Factors	T2DM		Total n (%)	χ^2 (df)	p value
	Yes (%)	No (%)			
Age Group					
41-50 years	12 (21.1)	45 (78.9)	57 (100.0)		
51-60 years	21 (21.9)	75 (78.1)	96 (100.0)	58.64 (3)	0.000
61-70 Years	35 (35.0)	65 (65.0)	100 (100.0)		
≥71 years	78 (67.2)	38 (32.8)	116 (100.0)		
Sex					
Male	69 (25.0)	207 (75.0)	276 (100.0)		
Female	77 (82.8)	16 (17.2)	93 (100.0)	97.14 (1)	0.000
Residence					
Rural	48 (25.4)	141 (74.6)	189 (100.0)		
Urban	98 (54.4)	82 (45.6)	180 (100.0)	32.53 (1)	0.000
Smoking					
Yes	114 (45.1)	139 (54.9)	253 (100.0)		
No	32 (27.6)	84 (72.4)	116 (100.0)	10.16 (1)	0.001
BMI (Kg/m^2)					
Normal (18.5-24.99)	41 (27.0)	111 (73.0)	152 (100.0)		
Overweight/Obese (≥23.00)	105 (48.4)	112 (51.6)	217 (100.0)	17.14 (1)	0.000
Duration of COPD					
<5 Years	69 (26.4)	192 (73.6)	261 (100.0)		
≥ 5 Years	77 (71.3)	31 (28.7)	108 (100.0)	64.29 (2)	0.000
Severity of COPD					
GOLD 1 (Mild)	9 (13.2)	59 (86.8)	68 (100.0)		
GOLD 2 (Moderate)	19 (18.8)	82 (81.2)	101(100.0)	74.51 (1)	0.000
GOLD 3 (SEVERE)	56 (51.9)	52 (48.1)	108 (100.0)		
GOLD 4 (Very Severe)	62 (67.4)	30 (32.6)	92 (100.0)		

82.8% of female study participants had T2DM as compared to only 25.0% of their male counterparts. 54.4% of study participants from urban area had T2DM against only 25.4% of study participants from rural area. Female sex and urban residence were found to be significant risk factors for T2DM among COPD patients (Table-2). Smoking history was significantly associated with higher COPD prevalence as 45.1% of study participants with Smoking history had T2DM as compared to 27.6% of non smokers (Table-2). BMI≥25.0 was found to be a significant risk factor for T2DM among COPD patients. 48.4% of overweight/obese and 27.0% of normal BMI study participants had T2DM respectively (Table-2). 71.3% of study participants with COPD history ≥ 5 years had diabetes and 26.4% with COPD history <5years had T2DM (Table-2). 67.4% of study participants with very severe COPD had T2DM followed by 51.9%, 18.8% and 13.2% who had severe , moderate and mild COPD had T2DM respectively (T2DM). Longer duration of COPD as well as increasing severity of COPD was found to be significantly associated with higher T2DM prevalence (Table-2). Descriptive statistics of one way ANOVA (Table-3) showing mean HbA1C among different grades of COPD severity and there is a statistically significant difference between groups as determined by one-way ANOVA (F = 46.45, p=0.000) (Table-4).

Table-3: Descriptive Statistics of One- way ANOVA between HbA1C as dependent variable and severity of COPD as independent variable. (n=369)

HbA1C

	n	Mean	Std. deviation	Std. Error	95%CI
Mild COPD	68	5.99	.635	.077	5.83-6.14
Moderate COPD	101	5.94	1.340	.133	5.68-6.21
Severe COPD	108	7.51	1.586	.153	7.21-7.81
Very Severe COPD	92	7.92	1.737	.181	7.56-8.28
Total	369	6.90	1.678	.087	6.73-7.07

Table-4: One- way ANOVA Statistics between HbA1C as dependent variable and severity of COPD as independent variable. (n=369).

HbA1C

	Sum of squares	df	Mean squares	F	Sig.
Between Groups	286.401	3	95.467	46.455	0.000
Within Groups	750.087	365	9.055		
Total	1036.488	368			

Mean plot of HbA1C against COPD severity (Fig-1) shows significant increase in severity with increasing mean HbA1C level from moderate to severe and very severe COPD.

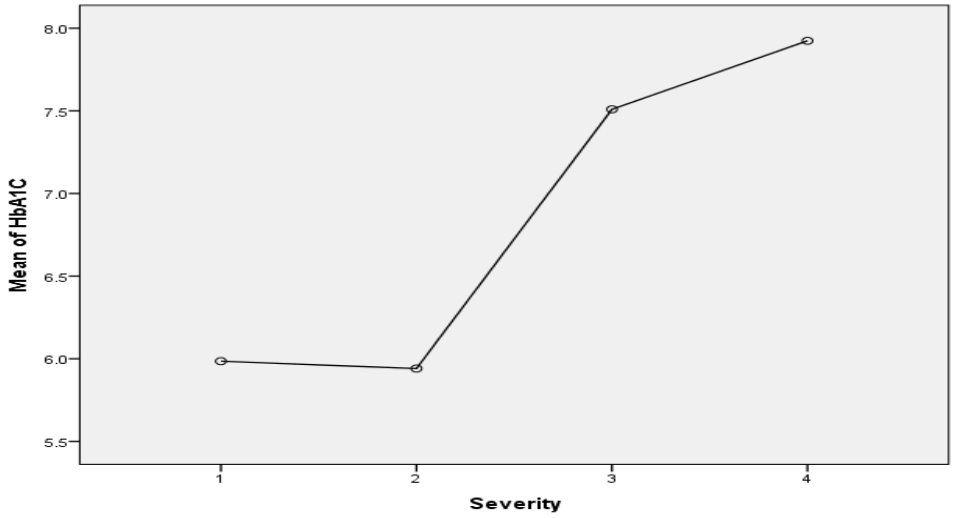

Fig-1: Mean plot of HbA1C against Severity of COPD (n=369)

1= Mild COPD, 2= Moderate COPD, 3= Severe COPD, 4= Very Severe COPD

One way ANOVA was further extended with "tukeys post hoc test" to do multiple comparisons and it revealed that the mean HbA1C was statistically higher among severe COPD (7.51±1.6%, p-0.000) and very severe COPD (7.92±1.73%, p-0.000) groups than mild (5.99±0.64%) and moderately severe COPD (5.94±1.34%) groups. There was no significant difference between mild & moderate severe COPD groups (p-0.997) as well as severe and very severe COPD groups (p-0.176) (Table-3 & Table-5).

Table-5: Multiple comparisons with Tukeys post hoc analysis of One- way ANOVA Statistics between HbA1C as dependent variable and severity of COPD as independent variable. (n=369).

Dependent Variable: HbA1C

Tukey HSD

(I) Severity	(J) Severity	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	.045	.225	.997	-.54	.63
	3	-1.524*	.222	.000	-2.10	-.95
	4	-1.939*	.229	.000	-2.53	-1.35
2	1	-.045	.225	.997	-.63	.54
	3	-1.569*	.198	.000	-2.08	-1.06
	4	-1.983*	.207	.000	-2.52	-1.45
3	1	1.524*	.222	.000	.95	2.10
	2	1.569*	.198	.000	1.06	2.08
	4	-.415	.203	.176	-.94	.11
4	1	1.939*	.229	.000	1.35	2.53
	2	1.983*	.207	.000	1.45	2.52
	3	.415	.203	.176	-.11	.94

1= Mild COPD, 2= Moderate COPD, 3= Severe COPD, 4= Very Severe COPD

Discussion

Present Cross-Sectional study was conducted to see the prevalence of T2DM among COPD patients. Total 369 study participants participated in study. In this study T2DM prevalence was found to be 39.6%. Our findings are slightly higher than the Ajit E et al[23] and Mahishale et al**[29]** who reported 23.05% and 25.63% respectively the prevalence of T2DM among COPD patients. However, few researchers from other countries reported that about 50.0% of COPD patients with acute exacerbation presents with high blood sugar**[30-32]**. About 1/5th of the study population were known T2DM patients and about 1/5th were newly diagnosed i.e they were unaware of their T2DM status. However, a lower prevalence 8.49% of newly diagnosed T2DM among COPD was reported by Ajit E et al[23]. The COPD as a risk factor for developing T2DM was reported by Rana JS et al**[33]** and Feary JR et al[34]. High prevalence of newly diagnosed T2DM in our study population may be because of the fact that more than half of the study population were from rural area having poor access to health care facilities resulting in non detection of T2DM.

In this study, increasing age was found to be a non modifiable and significant risk factor for T2DM among COPD patients. Increasing age as a significant risk factor for T2DM was also reported by few other researchers[**19, 36-37]**. In this study female gender was found to be another non modifiable risk factor for developing T2DM among study participants. Similar finding of female predominance of hyperglycemia was reported by Archana Har et al[38]. Contrary to our findings few other researchers reported a male preponderance of hyperglycemia[**19, 39-40]**. However, few researchers reported no effect of gender on the development of T2DM**[41-42]**. Study participants from urban area had significantly higher prevalence of T2DM than their rural counterparts. Ramachandran A et al**[39]** reported similar trend of higher T2DM prevalence among urban population. Recently published "STRiDE-1" study from South India also reported high prevalence of T2DM among urban population than rural population**[43]**. Study participants with Smoking history had higher prevalence of T2DM than their non smoker counterparts. High prevalence of T2DM among COPD patients with smoking history was

also reported by Ajit E et al[23]. Few large international trials namely the Zutphen study**[44]**, the Framingham Study[45] and the Israeli Study[46] also reported high prevalence of T2DM among smokers. Overweight and obesity was found to be significant risk factor for T2DM among study participants. Many other studies also reported higher prevalence of T2DM among overweight and obese people**[23,19,38,39,41]**. Long duration of COPD was significantly associated with increased risk of T2DM. This finding is in agreement with the finding reported by Ajit E et al[23]. T2DM was significantly associated with more severe disease among COPD patients. Significant high burden of severe COPD and frequent exacerbation among COPD patients with T2DM is a consistent finding. Researchers across the globe (Ajit E et al[23], Stojkovikj J et al**[47]**, The Fremantle Diabetes Study**[48]**, El-Habashy et al**[49]** have reported similar effect of T2DM on COPD severity.

Limitations of the study include non applicability of the results to general population because study setting is a tertiary health care facility which bound to get more complicated cases.

Conclusion

High prevalence of T2DM was found among COPD patients. Increasing age, female gender, urban residence and longer duration of COPD were significant non modifiable risk factors for T2DM among COPD patients. High BMI and Smoking were found to be significant modifiable risk factors for T2DM among COPD patients. More frequent screening of T2DM and good control of T2DM should be done because about 1/5th of the COPD patients had newly diagnosed T2DM and presence of T2DM significantly resulted in more severe disease.

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