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Original research article

ASSOCIATION BETWEEN TYPE 2 DIABETES MELLITUS AND THE SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PATIENTS AT A TERTIARY CARE CENTRE

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Abstract

Introduction: Non-communicable diseases (NCDs) such as cardiovascular diseases, stroke, and chronic respiratory diseases pose a significant burden on global health, with chronic obstructive pulmonary disease (COPD) being one of the leading causes of mortality among them. The prevalence of COPD continues to increase worldwide and is projected to be the third leading cause of death by 2030. According to World Health Organization (WHO) estimates, 65 million people have moderate-to-severe COPD worldwide. Mortality due to COPD in 2005 corresponded to 5% of all deaths globally.

Diabetes mellitus (DM) is an important and common comorbid condition associated with chronic obstructive pulmonary disease (COPD). The exact prevalence of DM in COPD patients among the Indian population is unknown. Coexisting DM is associated with poor outcomes in COPD patients and has a significant impact on lung function and the severity of the disease.

Aim: The aim of this study was to determine the prevalence of type 2 diabetes mellitus (DM) in chronic obstructive pulmonary disease (COPD) patients attending a tertiary care hospital and to assess its impact on the severity of the disease and exacerbations.

Methods: A cross-sectional study was conducted at a tertiary care center in Siddhartha Medical College, Vijayawada, from July to December 2023. Convenience sampling was used to study 400 patients attending the hospital for consultation. An interview schedule consisting of sociodemographic details was utilized. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria 2015 were used to diagnose COPD, and the World Health Organization (WHO) criteria were used to diagnose diabetes mellitus (DM).

Results: The prevalence of diabetes mellitus (DM) was 30% (120) among the 400 COPD patients studied. Among these, 28 patients (7%) were newly diagnosed with

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DM. The prevalence of DM in patients with mild, moderate, severe, and very severe COPD was 15%, 20%, 38%, and 32%, respectively. Patients in the DM group had a significant decline in lung function compared to those in the non-DM group, with a mean forced expiratory volume (FEV1) of 47.2 ± 4.0% versus 58.12 ± 3.2% (P = 0.001). Additionally, the majority of patients with DM (30%) were experiencing exacerbations, compared to 12% in the non-DM group.

Conclusion: Diabetes mellitus (DM) is a common comorbidity in patients with chronic obstructive pulmonary disease (COPD). A significant proportion of COPD patients are newly diagnosed with DM and are often unaware of their diabetic status. DM significantly affects the clinical course of COPD, with patients who have uncontrolled DM experiencing more severe COPD, poorer lung function, and more frequent exacerbations.

Keywords: Diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), forced expiratory volume (FEV1)

Introduction

Chronic obstructive pulmonary disease (COPD) and diabetes mellitus (DM) are common and often underdiagnosed medical conditions in India. COPD is a progressive, partially reversible airflow obstructive condition that poses a growing public health problem globally. In its advanced stages, COPD leads to severe disabilities and a poor quality of life. It was predicted that COPD would be the third leading cause of death worldwide by 2020, with Asian countries having three times the number of patients compared to the rest of the world. When considering mortality from comorbid conditions like DM, COPD has an even greater impact on health outcomes [1, 2].

COPD may be a novel risk factor for new-onset type 2 diabetes (T2DM) through various pathophysiological mechanisms, such as inflammation, oxidative stress, insulin resistance, weight gain, and altered adipokine metabolism. This risk exists regardless of the severity of COPD. T2DM is a common medical disorder and a leading cause of morbidity and mortality worldwide. Disturbances in glucose metabolism are more frequent in COPD patients than in non-COPD individuals. Nearly half of all COPD patients also suffer from other medical problems linked to diabetes, such as elevated blood pressure and high cholesterol levels, collectively referred to as "metabolic syndrome" [3, 4, 5]. This syndrome is a cause of various cardiovascular complications in COPD patients. Studies have shown that DM accelerates the decline in lung function compared to non-diabetics, and uncontrolled diabetes is associated with worse outcomes, including longer hospital stays and increased risk of death during COPD exacerbations [6, 7, 8].

In India, the prevalence of chronic obstructive pulmonary disease (COPD) is estimated at 3.67%, with about 15 million cases, where males and females contribute 9.02 million and 5.75 million cases, respectively. However, these figures may underestimate the true burden since questionnaire-based prevalence rates tend to be lower than those based on spirometry, which is the gold standard for diagnosing COPD. The discrepancy highlights the potential for significant under diagnosis and underscores the need for improved screening and diagnostic practices. Concurrently, India has experienced an accelerated epidemic of diabetes mellitus (DM) over the past 50-60 years. The national adult prevalence of DM is currently estimated at 8.3%. Given the country's large

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population, this prevalence translates to a substantial absolute number of diabetes cases. Consequently, India is burdened with the highest number of COPD and DM cases globally. The coexistence of these conditions poses a significant public health challenge, as both diseases contribute to increased morbidity and mortality rates [9-11].

Despite the known associations between COPD and DM, the exact prevalence of DM among COPD patients in the Indian population remains unclear. This gap in knowledge is critical because the coexistence of DM can exacerbate the clinical course of COPD, leading to more severe disease, poorer lung function, and more frequent exacerbations. Uncontrolled diabetes further complicates the management of COPD, resulting in longer hospital stays and higher risks of death during acute exacerbations. In a prospective Australian study, the Fremantle Diabetes Study, 125 patients with type 2 diabetes mellitus (T2D) and no history of lung disease were assessed by spirometry at baseline and re-evaluated seven years later. The key finding was that the average rate of decline in lung function, as measured by forced expiratory volume in one second (FEV1), was 71 ml/year, compared to an expected decline of 25-30 ml/year in healthy non-smokers. This suggests that exposure to elevated blood glucose levels may be a strong and consistent negative predictor of lung function decline, even after adjusting for baseline measurements and potential confounders [12-14].

The association between impaired lung function and diabetes is thought to result from biochemical changes in lung tissue and airway structures, involving mechanisms such as systemic inflammation, oxidative stress, hypoxemia, and direct damage caused by chronic hyperglycemia. These pathophysiological processes can lead to a more rapid decline in lung function in patients with diabetes compared to non-diabetic individuals. Consequently, diabetic patients appear to have an increased risk of developing several non-neoplastic lung conditions, including asthma and COPD.

In a retrospective study utilizing data from the Italian College of General Practitioners Health Search Database, it was found that patients with chronic obstructive pulmonary disease (COPD) exhibit a higher prevalence of diabetes mellitus (DM) compared to non-COPD individuals. Specifically, the prevalence of DM was reported as 10.5% in the general population versus 18.7% in patients with COPD. This association was further supported by a study conducted in Taiwan, which reported a higher risk of type 2 diabetes (T2D) in COPD patients compared to control subjects after adjusting for confounding factors. However, contrasting data exist in the literature, as demonstrated by Korean researchers who found no association between COPD and DM, possibly due to racial or nutritional differences or misclassification in diagnostic categories.

The exact reasons why patients with COPD are more affected by T2D than non-T2D subjects remain unclear. Several factors, including chronic hyperglycemia, inflammation or disease-related inflammation, oxidative stress, hypoxia, reduced physical activity, smoking habits, and corticosteroid treatment, may contribute to the higher prevalence of diabetes in COPD patients.

Furthermore, a retrospective analysis using data from the Italian College of General Practitioners Health Search Database indicated that COPD patients not only had an increased prevalence of cardiovascular diseases and T2D but also a low prevalence of metabolic syndrome. This suggests that COPD itself may act as a genuine risk factor for cardiovascular diseases and diabetes.

Several cross-sectional and prospective studies consistently report impaired pulmonary

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function and glucose intolerance among COPD patients. Prospective studies have shown that the development of DM is associated with accelerated rates of decline in pulmonary function, particularly at its onset. Additionally, analyses within the Normative Aging Study revealed negative associations between forced vital capacity (FVC) and insulin resistance, suggesting a correlation between insulin resistance and impaired pulmonary function. Longitudinal studies have also demonstrated an inverse association between pulmonary function and the risk of developing diabetes, even after adjusting for confounders. These findings collectively highlight the complex interplay between COPD and DM, suggesting bidirectional relationships that warrant further investigation to improve our understanding of these conditions and optimize patient management strategies.

Recent reports indicate that a pro-inflammatory state, which could be a common pathophysiological process for both chronic obstructive pulmonary disease (COPD) and type 2 diabetes (T2D), is present in overweight or obese pre-diabetic individuals as well as in the early stages of COPD. Biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) have been implicated in contributing to an altered metabolic state and insulin resistance. TNF-α, in particular, plays a role not only in inflammation but also in muscle wasting, which can lead to insulin resistance in skeletal muscle, sometimes associated with cachexia [14-17].

Conversely, a decrease in adiponectin levels, typically seen in pre-diabetic conditions, may contribute to pulmonary and vascular damage. Additionally, COPD may elevate oxidative stress levels due to a hypoxic state, further complicating the pathophysiological processes. This emerging understanding suggests that COPD can be considered a metabolic disease, sharing pathophysiological similarities with T2D. Therefore, it is essential to explore the various aspects of this association, particularly focusing on the hypothesized pathogenetic mechanisms involved, including the potential role of hyperglycemia as a linking factor between COPD and T2D. This review aims to shed light on these aspects and explore the possibility of a new conceptual understanding of the pathogenetic link between COPD and T2D. Given the high prevalence and the significant health impacts of both COPD and DM, it is essential to understand the interplay between these conditions better. Therefore, the objective of the present study was to screen COPD patients for DM systematically. This study aimed to determine the prevalence of type 2 diabetes mellitus in COPD patients attending a tertiary care hospital and to assess how diabetes affects the severity of COPD and the frequency and severity of exacerbations. By identifying the prevalence and impact of DM in COPD patients, the study aims to inform better management strategies and improve health outcomes for individuals suffering from these chronic conditions.

Aim

The aim of this study was to determine the prevalence of type 2 diabetes mellitus (DM) in chronic obstructive pulmonary disease (COPD) patients attending a tertiary care hospital and to assess its impact on the severity of the disease and exacerbations.

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Methods

A cross-sectional study was conducted at a tertiary care center in Siddhartha Medical College, Vijayawada, from July to December 2023. Convenience sampling was used to study 400 patients attending the hospital for consultation. An interview schedule consisting of sociodemographic details was utilized. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria 2015 were used to diagnose COPD, and the World Health Organization (WHO) criteria were used to diagnose diabetes mellitus (DM). A written informed consent was obtained from each participant before conducting the interview. The questionnaire used in the study was adapted from the GOLD criteria-2015, which is a widely recognized standard for diagnosing chronic obstructive pulmonary disease (COPD). According to the GOLD criteria, the spirometric criterion for diagnosing COPD involves assessing the post-bronchodilator value of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). This criterion helps in determining airflow limitation and classifying the severity of COPD based on FEV1/FVC ratio.

Results

Four hundred patients with COPD were included in the study. Among them, 328 (82.0%) were male and 72 (18.0%) were female. The mean age among study participants was 58.4 ± 11.6 years, with a mean body mass index of 24.2 ± 3.5. In the present study, the number of smokers among males was approximately 320 (80%), and none of the females reported smoking. About 20 (27.8%) female participants had a history of exposure to biomass fuel.

Among 400 study participants, 120 (30%) had diabetes mellitus (DM), with 28 patients (7%) being newly diagnosed with DM. The prevalence of DM in patients with mild, moderate, severe, and very severe COPD was 15%, 20%, 38%, and 32%, respectively. Patients in the DM group had a significant decline in lung function compared to those in the non-DM group, with a mean forced expiratory volume (FEV1) of 47.2 ± 4.0% versus 58.12 ± 3.2% (P = 0.001). Additionally, the majority of patients with DM (30%) were experiencing exacerbations, compared to 12% in the non-DM group.

Characteristics	Diabetics (n=120)	Non-diabetics (n=280)	P Value
Sex (male/female), n	96/24	232/48	0.310
Age (years), mean ± SD	57.54 ± 11.33	60.52 ± 11.38	0.172
BMI (kg/m^2), mean ± SD	24.84 ± 4.41	21.70 ± 3.46	0.067
Smoking (pack years), mean ± SD	13.58 ± 3.26	10.05 ± 4.91	0.001
Duration of COPD (years), mean ± SD	6.61 ± 1.99	6.74 ± 2.08	0.006
FEV1 (percentage predicted), mean ± SD	47.2 ± 4.0%	58.12 ± 3.2 %	0.001
Number of patients in exacerbation at the time of enrollment, n (%)	37 (31%)	48 (17 %)	0.007
HbA1c levels (mean ± SD)	9.5 ± 2.1	5.8 ± 1.7	0.0001

Note: SD: Standard deviation, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FEV1: Forced expiratory volume in 1s, HbA1c: Hemoglobin A1c.

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The table presents the demographic and clinical characteristics of diabetic and non-diabetic patients with chronic obstructive pulmonary disease (COPD). Among the diabetic group (n=120), 80% were male, while in the non-diabetic group (n=280), 83% were male, with no significant difference observed in sex distribution (p=0.310). The mean age of diabetic patients was 57.54 years (SD=11.33), slightly lower than that of non-diabetics, who had a mean age of 60.52 years (SD=11.38). Diabetic patients exhibited a higher mean body mass index (BMI) of 24.84 kg/m^2 (SD=4.41) compared to 21.70 kg/m^2 (SD=3.46) in non-diabetic patients. Smoking history, measured in pack years, was higher in diabetic patients (mean = 13.58, SD=3.26) than in non-diabetics (mean=10.05, SD=4.91), with a statistically significant difference (p=0.001).
The duration of COPD was similar between the two groups, with diabetics having a mean duration of 6.61 years (SD=1.99) and non-diabetics 6.74 years (SD=2.08). Diabetic patients had a significantly lower mean forced expiratory volume in 1 second (FEV1) at 47.2% (SD=4.0) compared to non-diabetic patients at 58.12% (SD=3.2), indicating poorer lung function in diabetics (p=0.001). Moreover, a higher proportion of diabetic patients experienced exacerbations at the time of enrollment (31%) compared to non-diabetics (17%) (p=0.007). Additionally, diabetic patients had higher mean hemoglobin A1c (HbA1c) levels (9.5%, SD=2.1) compared to non-diabetics (5.8%, SD=1.7), demonstrating poorer glycemic control among diabetic COPD patients (p=0.0001). These findings underscore the association between diabetes mellitus and worse clinical outcomes in COPD patients, highlighting the importance of comprehensive management strategies targeting both conditions to optimize patient care and outcomes.

Discussion

COPD represents a significant and escalating healthcare challenge globally, with India shouldering a considerable burden. Mortality rates attributed to COPD in India exceed those observed in the USA and Europe, a trend projected to intensify due to increasing rates of tobacco smoking and exposure to biomass fuel. The intricate interplay between COPD and the onset of type 2 diabetes mellitus (DM) is underscored by multifaceted factors including chronic inflammation, oxidative stress, and insulin resistance.
Simultaneously, there is a mounting prevalence of DM worldwide, with India identified as the epicenter of this diabetes epidemic. Contributing to this surge are lifestyle modifications, reduced physical activity, and the rising prevalence of obesity within the Indian populace. As India undergoes demographic shifts towards an increasingly elderly population, the coexistence of COPD and DM becomes more prevalent, exacerbating both morbidity and mortality rates. 0000000000Demographic and clinical profiles of diabetic and non-diabetic individuals diagnosed with chronic obstructive pulmonary disease (COPD) studied in our study. Among the diabetic cohort (n=120), 80% were male, mirroring the distribution observed in the non-diabetic group (n=280), where 83% were male, with no statistically significant difference noted in sex distribution (p=0.310). The mean age of diabetic patients was 57.54 years (SD=11.33), slightly lower than that of non-diabetic counterparts, who averaged 60.52 years (SD=11.38). Diabetic individuals displayed a higher mean body mass index (BMI) of 24.84 kg/m^2 (SD=4.41) compared to 21.70 kg/m^2 (SD=3.46) in non-diabetic

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counterparts. Notably, diabetic patients exhibited a greater smoking history, measured in pack years, with a mean of 13.58 (SD=3.26), compared to 10.05 (SD=4.91) in non-diabetic counterparts, demonstrating a statistically significant discrepancy (p=0.001). The duration of COPD demonstrated no discernible difference between the two groups, with diabetics reporting a mean duration of 6.61 years (SD=1.99) and non-diabetics reporting 6.74 years (SD=2.08). However, diabetic patients presented with a significantly lower mean forced expiratory volume in 1 second (FEV1) at 47.2% (SD=4.0), in contrast to non-diabetic patients at 58.12% (SD=3.2), indicative of poorer lung function among diabetics (p=0.001). Moreover, a higher proportion of diabetic individuals experienced exacerbations at enrollment (31%) compared to non-diabetics (17%) (p=0.007). Additionally, diabetic patients exhibited higher mean hemoglobin A1c (HbA1c) levels (9.5%, SD=2.1) compared to non-diabetics (5.8%, SD=1.7), signifying inferior glycemic control within the diabetic COPD cohort (p=0.0001). These findings underscore the association between diabetes mellitus and adverse clinical outcomes in COPD patients, emphasizing the imperative for comprehensive management strategies targeting both conditions to optimize patient care and outcomes.

For instance, a study conducted in Belgaum, India, reported a DM prevalence of 25.63% among COPD patients. Moreover, a notable proportion (8.49%) of diabetics were newly diagnosed, underscoring a lack of awareness regarding diabetic status. Notably, COPD patients exhibit an elevated risk for developing new-onset DM, as evidenced by various studies reporting heightened relative risks and odds ratios [17].

The current study marks a pioneering effort in actively screening COPD patients for diabetes mellitus (DM) in an Indian tertiary care hospital setting. Our findings revealed a DM prevalence of 25.63%, aligning with various reports from other nations. While the prevalence of DM in COPD patients varies across studies, our observed rate could be attributed to the predominantly older age of patients, with a history of smoking or prolonged exposure to biomass fuel. Additionally, the average duration of smoking among participants was 19 ± 8.2 years, primarily bidi smokers consuming raw, unfiltered tobacco. Systemic inflammation, characterized by elevated markers like C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6), plays a pivotal role in both COPD progression and insulin resistance development. Smoking, a key instigator of inflammation, poses a twofold higher risk of DM development among smokers compared to non-smokers. Recent literature reviews highlight the intricate interplay between smoking, obesity, and comorbidities, underscoring adipose tissue's role as a cytokine-producing site and the consequent exacerbation of pulmonary inflammation. The severity of systemic inflammation directly correlates with COPD severity, with moderate to severe COPD increasing the risk of DM development. Notably, airway inflammation's contribution to diabetes pathophysiology is evidenced by increased DM risk in patients with asthma or COPD [17, 18].

Our study also shed light on significant clinical implications, with DM significantly affecting COPD outcomes, including hospitalization rates and mortality. The risk of COPD-related death is notably elevated in individuals with diabetes, emphasizing the critical need for early DM detection and management in COPD patients. Notably, a substantial proportion of COPD patients in our study were newly diagnosed with DM, highlighting the necessity for routine DM screening in this population, particularly

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given the widespread use of high-dose inhaled and systemic corticosteroids.

Furthermore, our study identified a noteworthy subset of COPD patients with impaired fasting blood sugar levels (110-126 mg/dl), indicative of pre-diabetes. These individuals represent a high-risk group for future DM development, underscoring the importance of proactive screening and intervention strategies. With India bearing a substantial burden of both COPD and DM, particularly in rural areas with limited diagnostic facilities, early DM detection in COPD patients assumes paramount importance. Addressing the escalating DM epidemic necessitates comprehensive lifestyle interventions and improved access to healthcare services, crucial for mitigating the adverse impact of undiagnosed or poorly controlled DM on COPD outcomes, including exacerbations, hospitalizations, and mortality rates [18, 19].

Additionally, our study unveiled that COPD patients with comorbid DM displayed a significant decline in FEV1, prolonged COPD duration, and heightened rates of exacerbations, consistent with existing literature. The rapid deterioration of pulmonary function in diabetic individuals, particularly when glycemic control is suboptimal, is underscored by several investigations, including findings from the Fremantle Diabetes Study and El Habashy *et al*. [20, 21].

Despite the strengths of our study in comparing lung function and exacerbations between diabetic and non-diabetic COPD patients, limitations include a relatively small sample size and the single-center design, which may restrict generalizability. Furthermore, transient hyperglycemia and the administration of steroids may confound new DM diagnoses, although confirmation with HbA1C mitigates this concern.

Conclusion

Diabetes mellitus (DM) is a common comorbidity in patients with chronic obstructive pulmonary disease (COPD). A significant proportion of COPD patients are newly diagnosed with DM and are often unaware of their diabetic status. DM significantly affects the clinical course of COPD, with patients who have uncontrolled DM experiencing more severe COPD, poorer lung function, and more frequent exacerbations.

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