ORIGINAL ARTICLE

Association between Medication Adherence and Dyspnea Severity in Chronic Obstructive Pulmonary Disease Patients with Multimorbidity

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a chronic respiratory condition that is progressive and usually occurs with other health problems, poor adherence to medication, and high symptom burden. Comorbid conditions and poor adherence to maintenance therapy negatively impact functional outcomes and disease control in COPD patients. **Objective:** The objective of the study is to assess the burden of comorbidities and medication adherence and clinical outcomes related to dyspnea in patients with COPD and to find the association between medication adherence and severity of dyspnea in a tertiary care setting. **Materials and Methods:** This was a prospective observational study conducted over a period of 6 months among 153 physician-diagnosed COPD patients admitted to the inpatient and outpatient departments of a tertiary care teaching hospital in South India. Data related to demographic details, smoking history, alcohol use, severity of COPD, comorbidity profile, and treatment patterns were collected by interviewing the patients and reviewing their case records. Medication adherence was measured by means of the Morisky Medication Adherence Scale (MMAS-8) which is an 8-item licensed tool. The severity of dyspnea was graded according to the modified Medical Research Council (mMRC) dyspnea scale. Results were expressed in terms of descriptive statistics presenting frequencies and percentages. The Chi-square test was applied to find the association between categorical variables. A $P < 0.05$ was considered statistically significant. **Results:** Most participants were aged 60 years and above (70.6%) and male (97.4%). Current smoking was noted in 53.6% of patients; moderate-to-severe COPD cases predominating over GOLD stage II and III at 39.2% and 35.9%, respectively. Comorbidity burden was high, with 58.8% of patients having two or more comorbid conditions. The most prevalent comorbidities were hypertension (49.7%) and diabetes mellitus (37.9%). Long-acting muscarinic antagonist/long-acting beta agonist dual therapy was the main treatment in 30.1% and triple therapy in 28.1%. Only 15.7% of patients had high medication adherence, with 40.5% having low adherence. Most patients suffered from clinically significant dyspnea, with

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75.8% of the cohort having mMRC grades 2–4. There was a statistically significant association between medication adherence and mMRC dyspnea severity ($P < 0.001$) – poorer adherence linked with higher dyspnea grades. **Conclusion:** Patients with COPD at this tertiary care institution had a high multimorbidity burden, considerable symptom-related functional limitation, and mostly suboptimal medication adherence. This last factor was associated with worsening dyspnea severity – shining a spotlight on the need for adherence-focused interventions, inhaler counseling, and multidisciplinary management care for COPD patients.

Key words: Chronic obstructive pulmonary disease, clinical outcomes, comorbidity burden, dyspnea severity, medication adherence, modified medical research council scale, Morisky medication adherence scale-8, multimorbidity

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. In the present study, we investigated the relationship between COPD medication adherence and dyspnea-related health status, taking into consideration the potential mediating effect of dyspnea severity. We also examined the role of comorbidity burden in the relationship between medication adherence and clinical outcomes in a multimorbid COPD population. The following eight items comprise the instruments: Morisky Medication Adherence Scale (MMAS-8), dyspnea severity, modified Medical Research Council (mMRC) scale, comorbidity burden, clinical outcomes, and multimorbidity.

COPD is a chronic and progressive respiratory disease characterized by persistent airflow limitation, chronic respiratory symptoms, and recurrent exacerbations which contribute significantly to global morbidity and mortality. Major public health challenges and causes of death in the world, particularly in low- and middle-income countries, are still attributed to COPD where exposure to tobacco, biomass smoke, occupational pollutants, delayed diagnosis, and limited access to long-term respiratory care is highly prevalent. In India, COPD significantly adds to healthcare burden due to its association with frequent hospitalizations, impaired quality of life, reduced functional capacity, and increasing treatment-related costs.[1,2]

Though COPD traditionally has been perceived as a disease of the lungs, more contemporary views regard it as a multi-systemic disorder. For instance, hypertension, diabetes mellitus, ischemic heart disease, chronic kidney disease, osteoporosis, anxiety, and depression are among the most prevalent problems in COPD patients, which can independently raise symptom burden, exercise intolerance, risk of hospitalization, and overall prognosis. Multimorbidity also increases polypharmacy and treatment complexity, thereby worsening long-term disease management and negatively impacting medication adherence.[3,4]

Medication adherence is a big player in clinical outcomes in COPD. Maintenance therapy is defined as the regular and correct use of inhaled medications for symptom control and prevention of exacerbations. Optimal adherence to inhaled therapy is not achieved in routine clinical practice. This is especially true in the older population due to complex treatment regimens, poor inhaler technique, low health literacy, financial burden, and poor disease perception. Poor adherence has been associated with exacerbations of COPD, increasing dyspnea, higher rates of hospitalization, and decreasing quality of life in COPD patients.[5] Therefore, assessing adherence behavior is essential in COPD management.

This is because the spirometric severity itself does not adequately reflect the functional limitation and impairment of daily activities in the patient. The mMRC dyspnea scale is a simple tool and widely used to assess breathlessness-related functional disability in patients with COPD. Diminished exercise tolerance, poorer quality of life, and higher risk of exacerbations and hospitalizations are associated with higher grades of mMRC.[1,6] Assessment of symptom burden together with that of dyspnea severity, medication adherence, and comorbidity burden may therefore provide clinically meaningful insight into real-world COPD outcomes.

In resource-constrained settings of developing countries such as India, patients with COPD usually present moderate-to-severe disease, persistent smoking exposure, delayed healthcare-seeking behavior, and substantial multimorbidity. However, there is no information available on the combined assessment of comorbidity burden, medication adherence, and dyspnea-related outcomes in a tertiary care setting of a semi-urban/peri-rural population. There may be differences in terms of age groups and lifestyle factors that could influence disease severity, treatment patterns, and adherence behavior, and therefore overall clinical outcomes.

Therefore, the present study was undertaken to evaluate the demographic and clinical profile, comorbidity burden, medication adherence as per MMAS-8, and dyspnea severity by the mMRC scale among COPD patients at a tertiary care teaching hospital in South India. The study also aimed to assess the relationship between adherence status and severity of dyspnea, and differences among various age groups and lifestyle-related variables to find clinically important targets for pharmacist-led interventions and multidisciplinary COPD care.

MATERIALS AND METHODS

Study design and setting

This was a prospective observational study for 6 months in the inpatient and outpatient departments involved in the management of chronic respiratory diseases at a tertiary care teaching hospital in Madanapalle, Andhra Pradesh, India. The study was planned to assess the clinical profile, comorbidity burden, medication adherence, and dyspnea-related outcomes among patients with COPD under routine clinical practice conditions.

Study population

COPD in patients aged 40 years or older diagnosed by the treating physician and who received care during the study period was considered eligible for screening. Diagnosis could be confirmed through the case records, prescription charts, pulmonology/general medicine notes, and spirometric findings if available. The only other inclusion criteria were age 40 years or above and ability and willingness to provide informed consent and participate in the interview process. Exclusion criteria included alternative primary respiratory diagnoses and severe cognitive impairment. Critical illness precluding reliable data collection, duplicate admissions, and incomplete core clinical data were also grounds for exclusion.

Sample size and sampling technique

The formula used to estimate the minimum required sample size for the observational study was as follows.[7]

$$n = z^2 \times p \times q/d^2$$

Where:
n = required sample size
z = Z statistic corresponding to the desired confidence level (1.96 for 95% confidence)
p = anticipated prevalence (proportion)
q = 1 − p
d = absolute precision (margin of error)

Where Z = 1.96, *P* = 50%, q = 50%, and allowable error (d) = 10%. The calculated minimum sample size was about 96 participants. To allow for subgroup analysis and compensate for missing data, all eligible patients who presented during the study period were consecutively recruited. In total, 153 patients with complete analyzable data were included in the final analysis. Consecutive non-probability sampling was used.

Data collection

Data were collected using a structured case record form that was developed for the study. The information that was obtained included demographic characteristics, smoking and alcohol history, severity of COPD, comorbidity profile, pattern of respiratory treatment, medication adherence, and dyspnea severity. These were obtained through direct patient interviews and to enhance the reliability of the data were supported by case sheets, medication charts, physician notes, and investigation records.

COPD severity was documented by noting the GOLD staging stated in clinical records.[1] Comorbidity burden was noted by documenting the chronic conditions – hypertension, diabetes mellitus, ischemic heart disease, chronic kidney disease, anemia, osteoporosis, anxiety, and depression. Respiratory treatment regimens included short-acting bronchodilator therapy, long-acting muscarinic antagonist (LAMA) monotherapy, inhaled corticosteroid/long-acting beta agonist (ICS/LABA) therapy, LAMA/LABA dual therapy, and triple therapy.

Assessment of medication adherence

Medication adherence was assessed with the MMAS-8.[8] It was administered in accordance with authorized guidelines, and patients were classified as having high, medium, or low adherence based on standard scores. The items of the questionnaire are not to be reproduced in the manuscript since they are under copyright.

Assessment of clinical outcomes

The degree of dyspnea was evaluated by means of the mMRC dyspnea scale,[6] which grades breathlessness from 0 to 4 according to activity-related functional limitation; higher scores indicate greater symptom burden. This was done in the same patient interaction as that of the adherence assessment.

Variables assessed

The study variables were classified into the following domains: demographic, lifestyle, disease-related, treatment-related, adherence-related, and outcome-related. Smoking and alcohol use were grouped into current, former, or never users. The comorbidity burden was categorized as none, one, two, and three or more comorbidities. For statistical analysis, medication adherence and mMRC grades were treated as ordinal categorical variables.

Statistical analysis

The data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences software. The descriptive statistics included frequencies and percentages for the categorical variables and mean and standard deviation

Table 1: Baseline demographic and clinical characteristics of COPD patients

Variable	*n* (%)
Age group (years)	
40–49	14 (9.2)
50–59	31 (20.3)
60–69	48 (31.4)
70–79	41 (26.8)
≥80	19 (12.4)
Gender	
Male	149 (97.4)
Female	4 (2.6)
Smoking status	
Current smoker	82 (53.6)
Former smoker	53 (34.6)
Never smoker	18 (11.8)
Alcohol consumption	
Current use	56 (36.6)
Former use	27 (17.6)
Never use	70 (45.8)

COPD: Chronic obstructive pulmonary disease

Table 2: Disease severity and comorbidity profile among COPD patients

Variable	*n* (%)
GOLD stage	
Stage I	15 (9.8)
Stage II	60 (39.2)
Stage III	55 (35.9)
Stage IV	23 (15.0)
Comorbidity burden	
None	19 (12.4)
One	44 (28.8)
Two	53 (34.6)
≥3	37 (24.2)
Specific comorbidities	
Hypertension	76 (49.7)
Diabetes mellitus	58 (37.9)
Ischemic heart disease	25 (16.3)
Anemia	21 (13.7)

COPD: Chronic obstructive pulmonary disease

for continuous variables where appropriate. The Chi-square test was used to measure association between categorical variables. The relationship between age groups and severity of COPD and the adherence category according to MMAS-8 and dyspnea grade of mMRC was assessed. A $P < 0.05$ was taken as statistically significant.

Table 3: Treatment pattern, medication adherence, and dyspnea severity

Variable	*n* (%)
Treatment pattern	
Short-acting only	18 (11.8)
LAMA	14 (9.2)
ICS/LABA	32 (20.9)
LAMA/LABA	46 (30.1)
Triple therapy	43 (28.1)
MMAS-8 adherence category	
High adherence	24 (15.7)
Medium adherence	67 (43.8)
Low adherence	62 (40.5)
mMRC dyspnea grade	
Grade 0	9 (5.9)
Grade 1	28 (18.3)
Grade 2	47 (30.7)
Grade 3	44 (28.8)
Grade 4	25 (16.3)

LAMA: Long-acting muscarinic antagonist, ICS: Inhaled corticosteroid, LABA: Long-acting beta agonist, MMAS-8: Morisky medication adherence scale, mMRC: Modified Medical Research Council

Table 4: Association analyses among COPD patients

Association	χ^2	df	*P*-value	Cramer's V
Age versus GOLD	38.15	12	<0.001	0.29
MMAS versus mMRC	57.07	8	<0.001	0.43

MMAS-8: Morisky medication adherence scale, mMRC: Modified Medical Research Council, COPD: Chronic obstructive pulmonary disease

Table 5: Spearman correlation analysis of pack-year smoking exposure with COPD severity and dyspnea outcomes

Variables	Spearman's ρ	*P*-value
Pack-years versus GOLD stage	0.154	0.029
Pack-years versus mMRC score	−0.051	0.471

mMRC: Modified Medical Research Council, COPD: Chronic obstructive pulmonary disease

Ethical considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee before the initiation of any study-related procedures (2nd IRB MCPM/2025/PO15). Informed written consent was obtained from each participant before enrolment. Confidentiality of patients was

maintained by using only identification codes. The study was observational and did not interfere with the routine clinical management of patients in any way. All data collected were stored in electronic files with passwords and were available only to the investigators.

RESULTS

This study included 153 patients with physician-diagnosed COPD in the final analysis. Most participants were elderly, predominantly male, with significant burdens of smoking exposure, comorbidities, and moderate-to-severe disease severity.

Demographic and lifestyle characteristics

The participants had a mean age of 65.63 ± 11.63 years, with 69.8% of them being 60 years or older. The largest age group was 60–69 years (31.4%), followed by 70–79 years (26.8%). This is consistent with the well-established predilection of COPD for older populations. The study population showed marked male predominance. Males accounted for 97.4% (n = 149) of the cohort, and females only 2.6% (n = 4). In terms of smoking history, 53.6% were current smokers, 34.6% were former smokers, and only 11.8% had never smoked. All the female participants were non-smokers.

Alcohol consumption was exclusively reported among male participants. Current alcohol use was observed in 36.6% of the patients, and 17.6% were former alcohol users. Nearly half of the cohort, 45.8%, reported no alcohol consumption [Table 1].

COPD severity and comorbidity profile

Most patients had moderate-to-severe COPD. According to GOLD criteria, 39.2% of patients were classified as stage II and 35.9% as stage III. The cohort had 15.0% and 9.8% in stages IV and I, respectively. The enrolled patients had a substantial comorbidity burden: only 12.4% had no documented comorbidity; 34.6% had two comorbidities, and 24.2% had three or more comorbid conditions. Common comorbidities included hypertension, which affected 49.7% of the patients, diabetes mellitus (37.9%), ischemic heart disease (16.3%), anemia (13.7%), anxiety/depression (11.8%), heart failure (10.5%), chronic kidney disease (7.8%), and osteoporosis (6.5%) [Table 2].

Treatment patterns

The most commonly prescribed treatments were long-acting inhaled therapies. The most common treatment pattern was LAMA/LABA dual therapy (30.1%), followed by triple therapy (28.1%), and ICS/LABA therapy (20.9%). Short-acting bronchodilator-only therapy and LAMA mono therapy made up 11.8% and 9.2% of the prescriptions, respectively.

Medication adherence and severity of dyspnea

Medication adherence, as measured by the MMAS-8 scale, was generally suboptimal; only 15.7% of patients had high adherence, while 43.8% and 40.5% had medium and low adherence, respectively.

This population was characterized by marked functional limitation as assessed by the mMRC scale for dyspnea. 30.7%, 28.8%, and 16.3% of patients had mMRC grades 2, 3, and 4, which add up to 75.8% – more than three-fourths of the participants – clinically significant breathlessness [Table 3].

Association between age and COPD severity

The age group was significantly associated with COPD severity ($\chi^2 = 38.15$, df = 12, $P < 0.001$; Cramer's V = 0.29). Earlier age groups were predominantly in GOLD stages I and II, while with increasing age, stages III and IV became more common. Individuals 70 years of age and older had a higher percentage of severe disease compared to those who were younger [Table 4].

Association between medication adherence and dyspnea severity

The association of medication adherence with dyspnea severity was statistically significant ($\chi^2 = 57.07$, df = 8, $P < 0.001$; Cramer's V = 0.43). Most of the patients with low adherence were placed in higher mMRC grades (grades 3 and 4); those with high adherence were mostly found in lower dyspnea categories. None of the patients with high adherence, however, were placed under mMRC grade 4.

Association between smoking exposure and clinical outcomes

Spearman correlation analysis was used for assessing the relationship between pack-years of smoking (cumulative smoking exposure) and clinical parameters of COPD. A weak positive correlation was obtained for severity of dyspnea by GOLD stage with smoking in pack-years (Spearman's $\rho = 0.154$, $P = 0.029$). This simply implies that higher levels of cumulative tobacco exposure would tend to result in greater airflow limitation. On the other hand, pack-years did not correlate significantly with mMRC-assessed dyspnea severity (Spearman's $\rho = -0.051$, $P = 0.471$). This suggests that while pack-years of smoking would lead to increased severity in COPD, burden of dyspnea probably depends on additional factors such as adherence to medication, burden of comorbidities, and general functional status [Table 5].

DISCUSSION

This could be due to regional smoking habits, occupational exposure patterns, health-seeking conduct, and possible underdiagnosis among females. The low percentage of females may also show that COPD due to exposure to biomass fuel is not adequately identified in clinical practice, although its contribution to the disease burden in developing countries is well established. These findings indicate that the high percentage of male participants (97.4%) in this study is higher than that in many other recent COPD cohorts.[9-11] Poorer adherence was significantly associated with higher mMRC dyspnea grades, suggesting an important relationship between medication-taking behavior and symptom burden.[5,12]

The study population was mostly elderly, with over 60 years in most patients. This finding could be due to the chronic and progressive nature of COPD. This is a disease in which cumulative exposure to tobacco smoke, occupational pollutants, and environmental risk factors leads to progressive airflow limitation over time. Similar age distributions have been reported in studies of COPD in India and internationally. As disease prevalence and severity increase with age, pulmonary reserves decrease, and exposure to inhalational risk factors becomes long in the tooth.[1,11]

This marked male predominance observed in the present study also agrees with epidemiological data from many Indian settings, as smoking rates remain substantially higher among men compared with women in those areas.[9]

Smoking was the most prominent exposure pattern in this cohort; most participants were current or former smokers. This finding further emphasizes the established role of tobacco exposure as the primary modifiable risk factor for COPD development and progression. This finding is consistent with other studies that demonstrate the role of tobacco exposure as the primary preventable risk factor in the development and progression of COPD.[1,13]

All women participants were non-smokers. This finding probably reflects local sociocultural patterns in the rural and semi-urban South Indian populations. Active smoking among women is rare in these areas. Even though the number of female participants was small, this observation underscores the possibility that non-smoking-related exposures may contribute to the occurrence of COPD among women in similar settings. Such exposures include passive smoke exposure, biomass fuel exposure, and household air pollution.[9,10]

Most patients presented with moderate-to-severe COPD, with the largest proportion falling within GOLD stages II and III. That distribution could reflect somewhat delayed healthcare-seeking behavior and diagnosis since most patients were referred from the districts to tertiary care centers after substantial progression of symptoms and functional impairment. Such findings have been documented in low-and middle-income countries where, due to limited awareness of early symptoms and access to spirometric screening, COPD often goes underdiagnosed and treatment is initiated late.[14,15] The preponderance of moderate-to-severe disease falls in line with observed prescribing patterns: The dual bronchodilator and triple inhaled therapy are both frequently prescribed – as recommended in modern treatment guidelines for symptomatic patients at increased risk of disease progression and exacerbations.[1]

This is a clear demonstration of the fact that 58.8% of patients had two or more comorbidities, which is an emerging challenge in multimorbidity for the COPD management population.[3,16] Comorbidities can increase healthcare utilization through competing treatment priorities and medication burden, which in turn reduces adherence.[4] High prevalence of hypertension and diabetes, nearly half and one-third of the patients, respectively, suggests chronic disease management models that are integrated and not specific to a single disease in this population.[1,4]

Medication adherence as per the MMAS-8 scale was mostly medium to low; high adherence was attained in a small percentage. This finding was in accordance with earlier reports of poor adherence to inhaled COPD therapy in routine clinical practice. Factors that can contribute to suboptimal adherence behavior include the following: The chronic nature of COPD, long-term use of inhalers, polypharmacy, improper inhaler technique, the chronic nature of COPD, long-term use of inhalers, polypharmacy, improper inhaler technique, financial burden, low health literacy, and poor insight into symptoms. Poor adherence is clinically relevant because inadequate maintenance therapy can lead to persistent airway obstruction, worsening hyperinflation, increased exacerbation frequency, and progressive functional decline.[5,12]

The study also showed a high symptom burden since most patients fell under mMRC grades 2–4, which means a clinically significant limitation of activity due to breathlessness. Dyspnea is one of the most disabling manifestations of COPD and has a huge impact on daily functioning, exercise capacity, and quality of life. There was a statistically significant association between medication adherence and mMRC dyspnea severity. More specifically, higher grades of mMRC dyspnea were mostly found among low adherent patients, while the lower grades of dyspnea were observed in highly adherent patients. This finding underscores it as a clinically relevant factor in controlling symptoms and optimizing functional outcomes. Poor adherence may decrease the effectiveness of bronchodilator therapy, leading to persistent airflow limitation and worsening exertional breathlessness.[5,6,12]

The striking association between increasing age and higher GOLD stages may also reflect the age-related decline in

respiratory reserve as well as the delayed diagnosis in older individuals. Patients in the advanced stages of the disease often experience overlapping symptoms from cardiovascular disease, frailty, and reduced physical activity, which makes it more challenging to detect the disease at an early stage.[17]

The findings highlight the continued burden of tobacco-related COPD in India from a public health perspective and support the need for early case detection, tobacco cessation services, and regular adherence monitoring. Because this cohort has high rates of multimorbidity and poor adherence, it is suggested that educational interventions led by pharmacists and structured inhaler training programs in respiratory clinics may be a cost-effective approach to improving disease control and reducing healthcare utilization.

Strengths

This study has a few optimal points. It first evaluated the demographic features, multimorbidity burden, medication adherence, and dyspnea severity in a real-world tertiary care COPD population altogether. It used validated instruments including the MMAS-8 and mMRC scale for outcome assessment. It explored clinically relevant associations between adherence behavior and the burden of symptoms, providing evidence that may support targeted pharmacist-led interventions in routine practice.

Limitations

The study was carried out at a single center; hence, its findings cannot be generalized to all community populations. The number of female patients was quite low to draw any meaningful conclusions in the subgroup analysis based on gender. Dyspnea and medication adherence were measured on self-reported scales and hence are prone to recall and response biases. Detailed spirometric parameters and longitudinal exacerbation outcomes were not available in some patients. These limitations should be borne in mind while interpreting the results of the study.

CONCLUSION

COPD patients in this tertiary care cohort demonstrated major multimorbidity, moderate-to-severe disease burden, marked limitation of daily activities due to symptoms, and mostly suboptimal adherence to prescribed medications. Poor adherence was significantly associated with worsening severity of dyspnea, a marker that underlines the importance of interventions focused on adherence and strategies for the multidisciplinary management of COPD. Counseling and inhaler education carried out by pharmacists might be quite impactful in improving long-term clinical outcomes for people with COPD.

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