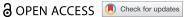


ORIGINAL ARTICLE



Determinants of poor chronic obstructive pulmonary disease control

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ABSTRACT

Uncontrolled COPD has been associated with reduced health-related quality of life, activity impairment, and increased use of healthcare resources. However, limited research is available on the factors associated with poor disease control in COPD patients. This study aimed to explore the factors associated with poor disease control in patients with COPD. The current cross-sectional study was conducted on patients with COPD who attended outpatient respiratory clinics at two major hospitals in Jordan. Information about disease and medication-related characteristics was collected through patient interviews and medical files. Validated instruments, including the 4-item medication adherence scale and the hospital anxiety and depression scales, were used to assess medication adherence, anxiety, and depression among the study participants. COPD severity was assessed using the GOLD classification criteria. Ordinal regression analysis was conducted to explore the variables associated with poor COPD control. In total, 702 patients participated in the study, with a median (interquartile range) age of 68 years (58-77). According to the GOLD report, most of the participants were in the B group (low risk/high symptoms; 40.2%), followed by the D group (high risk/high symptoms; 28.2%). Older age, higher depression scores, and a higher number of prescribed medications were associated with poorer COPD control, while not receiving LAMA (long-acting muscarinic antagonists) was associated with better control. Future mental health care initiatives should address the prevalence of depression symptoms in COPD patients and manage them effectively to improve COPD control and prevent further complications, with special attention to older patients, those receiving multiple medications, and those using LAMA.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic, incurable respiratory condition that affects around 13.1% of the global population [1]. In 2019, the World Health Organization rated COPD as the third leading cause of death, accounting for 6% of the world's total deaths. Additionally, nearly 90% of COPD deaths in those under 70 years of age occur in middle-income countries, including lowand Jordan [2].

COPD is a slowly progressive disease characterized by impaired pulmonary function and airway obstruction, with cough, shortness of breath, and sputum production being the most common symptoms [3,4]. Uncontrolled COPD has been associated with reduced health-related quality of life (HRQOL), greater work productivity and activity impairment, and increased use of healthcare resources [5,6].

Despite the availability of effective medications to manage COPD, many patients still experience episodes of symptoms exacerbations that worsen acutely, which reflects poor disease control and contributes to increased morbidity, mortality, and healthcare expenditures [7]. To develop effective strategies for better disease management, it is essential to identify the factors associated with poor COPD control. The literature reported inconsistent findings regarding the contributing factors of poor disease control among patients with COPD. A study conducted in Korea reported that female gender, higher COPD grade, and a higher number of exacerbations in the preceding year were significant predictors of COPD exacerbations [8]. An earlier systematic review identified airway obstruction, history of previous exacerbations, age, and smoking as the most common predictors of COPD exacerbations [9]. In a prospective cohort study conducted in Sweden, COPD patients with comorbid heart disease were found to have a significantly higher symptom burden [10].

The diversity in the factors associated with COPD control necessitates further research to reduce this variability and reveal the factors associated with uncontrolled COPD. Understanding local factors affecting COPD control is particularly crucial in lowincome countries like Jordan, where limited healthcare resources and cultural or socioeconomic barriers can significantly impact disease management. By identifying these specific factors, the findings of this study can help develop tailored interventions that address the unique challenges faced by patients in Jordan, ultimately improving disease control and reducing variability in treatment outcomes. To date, no studies have been conducted in Jordan to evaluate this issue. Therefore, the current study aimed to evaluate COPD control status and identify the factors associated with poorly controlled disease in the Jordanian population. The findings are expected to contribute to the development of effective strategies that improve COPD control and address the barriers to optimal disease management.

2. Materials and methods

2.1. Study design and participants

The present cross-sectional study followed the methods used by Jarab et al. [11] and was conducted on patients with COPD who attended outpatient respiratory clinics at King Abdullah University Hospital (KAUH) and Royal Medical Services (RMS). Participants who were 18 years or older, had a confirmed diagnosis of COPD for at least 6 months, and had been receiving stable COPD treatment for at least 6 weeks were eligible for inclusion. Patients with congestive heart failure, cognitive impairment, severe disease, or other pulmonary conditions were excluded from the study. Eligible patients were assured of the confidentiality and anonymity of the collected data, and they were informed that participation was voluntary and they had the right to refuse participation or withdraw from the study at any time.

2.2. Research ethics and patient consent

Ethical approval was obtained. All methods were performed in accordance with the relevant guidelines and regulations. Patients who agree to participate had to sign an informed consent form.

2.3. Study instruments and data collection

Information on age, gender, education level, income, smoking status, marital status, living conditions, living area, and pet ownership were collected using a custom-designed questionnaire. Patient interviews and medical records were used to collect data on disease-related and medication-related characteristics, including disease duration, the number of previous exacerbations in the past year, packs smoked per year, comorbidities (e.g. hypertension, heart diseases, obesity and diabetes), the number of COPD and total medications, use of inhaled corticosteroids, oral steroids, long-acting beta-2 agonists (LABA), longacting muscarinic antagonists (LAMA), short-acting beta-2 agonists (SABA), long-term oxygen therapy, concerns about medication side effects, inhaler technique, patients' evaluation of drug effectiveness, anxiety and depression levels, medication adherence, and GOLD disease severity. Symptom burden was assessed using the Modified British Medical Research Council (mMRC) Questionnaire and COPD Assessment Test (CAT). The final ABCD grouping, as suggested by the Global Initiative for Obstructive Lung Disease (GOLD), was used to categorize COPD severity into four groups: Group A (low risk/low symptoms), Group B (low risk/high symptoms), Group C (high risk/low symptoms), and Group D (high risk/high symptoms) [12]

2.3.1. The validated Arabic version of the 4-item medication adherence scale

The questionnaire contains four items, each with two response options: yes or no, with a score of one for each 'yes' response [13]. It assesses patient nonadherence in several ways, including forgetting to take medication, carelessness about taking medications, stopping medication when feeling better, and stopping medication when feeling worse. A score of zero indicates high adherence, a score of 1 or 2 indicates moderate adherence, and a score of 3 or 4 indicates low adherence. For analysis purposes, patients were categorized into two groups: those who scored zero were considered adherent, and those who scored between 1 and 4 were considered non-adherent.

2.3.2. The appropriate technique for using inhaler

The patients were asked to describe how they use their inhaler devices, and their responses were assessed using a validated checklist adapted from the German Respiratory League's recommendations to determine if they were using their inhalers correctly [14,15] Previous studies have demonstrated the impact of the correct inhaler technique on disease management [16,17].

2.3.3. Hospital anxiety and depression scale (HADS)

In 1983, the HADS was developed as a reliable and valid tool for detecting depression and anxiety in hospital outpatient settings [18]. The 14-item test yields two separate scores: one for anxiety and one for depression. Each item is graded on a scale of 0 to 3 (no impairment) with a maximum score of 21 for either anxiety or depression. A score of 11 or above on either scale indicates a clear case of anxiety, depression, or both [19]. The validated Arabic version of this instrument was utilized in this study [20].

2.4. Data analysis

Data were analyzed using the Statistical Package for the Social Science (SPSS) software program, version 27 (IBM, Armonk, NY, USA) [21]. Descriptive statistics were used to characterize the sample population, and frequency tables were employed to describe nominal and ordinal variables as frequencies and percentages. Q-Q plots indicated that the data were not normally distributed; therefore, continuous data were presented as medians with interquartile ranges (IQR). Multivariate ordinal regression was conducted to explore the variables associated with the dependent variable, COPD control in this study. The significance level was set at a P-value of < 0.05.

3. Results

A total of 702 patients participated in the study. The median (IQR) age was 68 years (58-77). The majority of the participants were male (78.6%), married (91.5%), smokers (58%), not living alone (93%), and living in urban areas (86.9%). Nearly half of the participants had a low income (<500 JD) (47%). More details about the socio-demographic characteristics of the study sample are available in Table 1.

As shown in Table 2, the majority of the participants had hypertension (72.6%), diabetes (50.4%), were receiving inhaled corticosteroids (68.4%), and believed their medications were effective(59%). Although most of the participants did not suffer from anxiety (59%), 54.7% were depressed. Furthermore, the majority of the participants were non-adherent to COPD medications (67.9%). The median inhaler score was 91.4% (IQR: 74.4-100), indicating good knowledge of the appropriate use of inhalers among the study participants. According to the GOLD disease severity, most participants were in the B group (40.2%), followed by the D group (28.2%).

As shown in Table 3, the results of the ordinal regression revealed that older age (coefficient = 0.033, 95%CI: 0.021–0.045, p < 0.001), and a higher number of prescribed medications (coefficient = 0.083, 95%CI: 0.003–0.163, p < 0.05) were associated with higher disease severity and poorer control. Additionally, a higher depression score was significantly associated with an increase in COPD severity (coefficient = 0.095, 95%CI: 0.046-0.144, p < 0.001), indicating that for each one-unit increase in the depression score, the log-odds of being in a higher COPD category increase by 0.095, holding all other variables constant. On the other hand, not receiving LAMA (coefficient = -0.318, 95%CI: -0.607-0.030, p <0.05) was associated with better COPD control.

4. Discussion

Poor disease control among COPD patients is a serious problem that impacts many aspects of their lives, highlighting the importance of investigating the factors contributing to uncontrolled COPD, which was the aim of the present study. According to GOLD

Table 1. Socio-demographic characteristics of the study participants (n = 702).

Variable		Median (25 th -75 th quartiles)	Frequency (%)
Age (years)		68 (58–77)	
Gender	Male		552 (78.6%)
	Female		150 (21.4%)
Educational level	Low		252 (35.9%)
	Moderate		228 (32.5%)
	High		222 (31.6%)
Average monthly income	less than 600 JD		330 (47.0%)
	600-1000 JD		290 (41.3%)
	more than 1000 JD		82 (11.7%)
Material status	Married		642 (91.5%)
	Other		60 (8.5%)
Smoking	Former smoker		295 (42.0%)
	Smoker		407 (58.0%)
Packs smoked per year		61.6 (44.1–78.3)	
Living conditions	Alone		49 (7.0%)
	Not alone		653 (93.0%)
Living area	Rural area		92 (13.1%)
	Urban area		610 (86.9%)
Having pets	No		636 (90.6%)
	Yes		66 (9.4%)

JD: Jordanian dinar.

Table 2. Disease and medication characteristics of the study participants (n = 702).

Variable			Median (IQR)	N (%)
Median disease duration (year)			4 (2–5)	
Post bronchodilator FEV1%			73% (67%-78%)	
Number of exacerbations in the past year			2 (1–3)	
Comorbidities	Hypertension		510 (72.6)	
	Heart diseases			366 (52.1%)
	Obesity			187 (26.6%)
	Diabetes			336 (47.9%)
Number of COPD medications			2 (2-2)	
Number of total medications			5 (3–6)	
Inhaled corticosteroids				480 (68.4%)
Oral steroids				24 (3.4%)
LABA				430 (61.3%)
LAMA				306 (43.6%)
SABA				138 (19.7%)
Medication combinations		LAMA		128 (18.2%)
		LAMA and LABA		30 (4.3%)
		LAMA, LABA and ICS		148 (21.1%)
Do you use long-term oxygen therapy?			56 (22.2%)	
Do you have concerns about the	ne side effects of COPD medication?	No		594 (84.6%)
		Yes		108 (15.4%)
Inhaler score percent			91.4 (74.4–100)	
Self-evaluation for COPD medication effectiveness		Low		54 (7.7%)
		Moderate		414 (59.0%)
		High		234 (33.3%)
Anxiety level		Normal		414 (59.0%)
		Abnormal		288 (41.0%)
Depression level		Normal		318 (45.3%)
		Abnormal		384 (54.7%)
Medication adherence		Non-adherent		477 (67.9%)
		Adherent		225 (32.1%)
GOLD disease severity group		Α		114 (16.2%)
		В		282 (40.2%)
		C		108 (15.4%)
		D		198 (28.2%)

FEV1: forced expiratory volume in one second, COPD: chronic obstructive pulmonary disease, LABA: long-acting B2 agonist, LAMA: long-acting muscarinic antagonist, SABA: short-acting B2 agonist, ICS: inhaled corticosteroid.

Table 3. Ordinal regression of variables associated with COPD control.

Variable		Ordinal regression coefficient	P- value	95% Confidence Interval	
				Lower Bound	Upper Bound
Age		0.033	<0.001**	0.021	0.045
Anxiety score		0.007	0.687	-0.029	0.043
Depression score		0.095	<0.001**	0.046	0.144
Disease duration		0.036	0.141	-0.012	0.083
Number of total med	lications	0.083	0.042*	0.003	0.163
Marital status	Married vs. Others	-0.483	0.057	-0.979	0.014
Receiving LAMA	No vs. Yes	-0.318	0.031*	-0.607	-0.030
Receiving LABA	No vs. Yes	0.112	0.472	-0.193	0.417
Antibiotics use	No vs. Yes	-0.506	0.208	-1.293	0.281
Diabetes	No vs. Yes	-0.098	0.562	-0.431	0.235
Hypertension	No vs. Yes	-0.295	0.092	-0.638	0.048
Heart diseases	No vs. Yes	0.055	0.739	-0.267	0.377

LAMA: long-acting muscarinic antagonist, LABA: long-acting B2 agonist.

classification criteria, more than one-third of the patients in the study were group B, followed by group D, indicating a notable prevalence of uncontrolled COPD. The present investigation identified several key factors associated with f COPD control, including age, depression, the total number of medications, and LAMA use.

Based on the GOLD disease severity classification, the majority of participants in our study were categorized into group B (40.2%), followed by group D (28.2%), which aligns with findings from a study conducted in the United States [22]. However, when comparing our findings with studies from India [23],

Thailand [24], and Spain [25], different patterns emerge. In those studies, most COPD patients were classified in GOLD group A, with approximately onethird falling into stage B. Notably, a study from Taiwan reported that the vast majority of COPD patients were in group A (73.4%), while only 20.2% and 4.6% were in groups B and D, respectively [26]. This discrepancy our study participants, suggests that a predominance in groups B and D, experience a higher symptom burden. Therefore, it is essential to develop individualized COPD management protocols tailored to the specific needs and preferences of each patient. To achieve this, it is imperative to

^{*} Significant at p < 0.05, ** Significant at p < 0.01.

investigate the factors hindering optimal COPD control status.

Despite a moderate to high self-evaluation of medication effectiveness, most participants were nonadherent to COPD medications. While patients may recognize the benefits of their treatment, a lack of understanding about the long-term benefits of medication adherence could contribute to inconsistent use. Additionally, poor medication adherence may result from factors such as medication costs, limited availability, or social challenges like low socioeconomic status. These factors should be carefully considered in future tailored interventions aimed at improving adherence in COPD management.

Consistent with earlier research findings [9,27], the current study found a strong relationship between older age and higher COPD severity, manifested by an increased risk of exacerbations and a higher symptom burden. Aging is associated with elevated levels of inflammation, oxidative stress, and a decline in immune system function. These age-related physiological changes may contribute to increased disease activity and greater susceptibility to exacerbations, ultimately leading to poorer disease control among individuals with COPD [28]. Future COPD management strategies should focus on reducing exacerbation rates and alleviating symptom severity in older patients. This may involve assessing the effectiveness of vaccination programs, optimizing pharmacological regimens, enhancing respiratory rehabilitation approaches, improving disease monitoring, and developing interventions specifically tailored to meet the needs of older adults.

The findings of the current study indicated that COPD patients with depression had more severe disease than those without. In general, COPD patients are more likely to experience anxiety, stress, and depression, all of which can exacerbate COPD symptoms and negatively impact disease progression [29,30] Previous studies have found that depression is significantly associated with a higher risk of acute exacerbations in patients with COPD [31,32]. Notably, fewer than one-third of COPD patients with coexisting symptoms of anxiety or depression receive adequate treatment. This is often due to a lack of awareness about antidepressant drug therapies, poor treatment adherence, and limited mental health resources. These issues can have serious consequences, including hindering effective COPD management and increasing healthcare utilization [33,34]. Therefore, greater attention from mental healthcare providers is essential to improving COPD control in patients with psychological comorbidities. Efforts should also be made to identify and address the barriers that prevent mental health support in this population.

In the current study, a significant association was observed between the total number of medications

taken and the severity of COPD. A study conducted in the United States reported that both higher medication regimen complexity and a greater number of medications were significantly associated with poorer COPD control [35]. Similarly, an Italian study found that hospitalized COPD patients experiencing acute exacerbations were more likely to be affected by polypharmacy [36]. This association may suggest that a limited number of medications is insufficient to manage more advanced stages of the disease, as greater severity often requires a more intensive pharmacological approach. In addition, the use of multiple medications may also reflect the presence of comorbid conditions or complications that necessitate further treatment. Additionally, LAMA use was associated with poorer disease control in this study, possibly reflecting greater disease severity in those prescribed LAMA. It is likely that patients who did not receive LAMA had less severe or earlier-stage COPD, which could explain better disease control compared to those prescribed LAMA. This finding does not suggest that LAMAs are ineffective, but rather that patients requiring LAMAs may have more challenges in managing their disease due to its severe or advanced state. Given the cross-sectional design of our study, future prospective or randomized controlled trials are warranted to further investigate the effects of polypharmacy and LAMA use on COPD control. Such studies would help establish causal relationships and provide a deeper understanding of the factors that contribute to improved management.

Based on the study findings, healthcare providers should recognize that older patients, those with higher depression scores, and those on multiple medications are at greater risk of poor COPD control. This emphasizes the importance of individualized treatment plans that address not only disease severity but also mental health and medication burden. Integrating mental health support, such as depression screening and psychological care, should be a core part of COPD management, especially for older patients. The study also revealed that not receiving LAMA was associated with better COPD control, likely because patients prescribed LAMA tend to have more severe disease. Therefore, healthcare providers should pay special attention to patients receiving LAMA therapy, acknowledging that these patients may require more intensive management due to their higher disease severity. Healthcare policies should prioritize access to mental health services and essential medications, including LAMAs for high-risk patients. Additionally, enhancing provider training and improving coordination between primary care providers, pulmonologists, and mental health professionals will be essential in addressing both the physical and psychological needs of patients with COPD.

4.1. Study limitations

While the present study utilized a large sample to provide valuable insights into the factors associated with poor COPD control, it is important to acknowledge some limitations that may affect the interpretation of the findings. First, the cross-sectional design limits the ability to establish causal relationships between variables or assess outcomes over time. Second, the study was conducted at only two hospital sites, which may limit the generalizability of the results to other settings or populations. Additionally, although convenient sampling allowed for the recruitment of a sufficient number of patients within the available time and resources without disruptions to patient care and clinic flow, this technique may introduce selection bias, as the sample may not fully represent the broader COPD population. Lastly, the use of self-report measures in the survey may have exposed responses to social-desirability bias, potentially affecting the accuracy of some findings

5. Conclusions

The current study showed a high prevalence of poor disease control among patients with COPD, with age, depression, the number of prescribed medications, and LAMA use identified as main factors associated with poorly controlled COPD. Clinicians should consider these factors when developing individualized interventions aimed at improving disease control and overall health outcomes among patients with COPD. Future mental health programs should also address the psychological symptoms commonly experienced by COPD patients, particularly depression, and ensure these are effectively managed to enhance COPD control and prevent further complications, particularly in older patients and those receiving LAMA therapy or multiple medications, as they may be at higher risk for poor disease control.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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