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Original Research Article

A cross-sectional study on the impact of methylxanthines, corticosteroids, and antibiotics on COPD symptoms: Assessment using CAT, mMRC, and GOLD criteria

Krishna Kumar Dhakchinamoorthi[1]*, Kadhiravan Suseelan[1], Karthick Sivanantham[1], Gokulalakshmi Moorthy[1], Balaji Manickam[1], Sivashanmugam Muruganandham[2]

[1]Dept. of Doctor of Pharmacy (Pharm.D), Government Medical College Hospital, Tiruppur, Tamil Nadu, India
[2]Dept. of General Medicine, Government Medical College Hospital, Tiruppur, Tamil Nadu, India

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a long-term inflammatory lung condition marked by irreversible airflow limitation. This study aimed to assess the effectiveness of a combination therapy—methylxanthines, corticosteroids, and antibiotics—on symptom relief and exacerbation frequency in hospitalized patients with COPD, using the COPD Assessment Test (CAT) and the modified Medical Research Council (mMRC) dyspnea scale.
Materials and Methods: A six-month cross-sectional observational study was conducted at Government Medical College Hospital, Tiruppur, with prior approval from the Institutional Ethics Committee. A total of 120 hospitalized patients provided informed consent and were evaluated using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification system.
Results: Among the participants, 49% were aged between 46 and 60 years. Initially, 86% had high CAT scores (21–30), which improved to a moderate range (11–20) in 90% of patients following treatment. Most patients reported mMRC grade 3 breathlessness before therapy, which improved to grade 2 afterward. In the previous year, 87% had experienced exacerbations, and 82% required hospitalization. Based on improvements in CAT and mMRC scores, the majority of patients shifted from GOLD Group C (severe) (85%) to Group B (moderate) (92%) after treatment, showing a statistically significant change ($p < 0.001$).
Conclusion: The combination of methylxanthines, corticosteroids, and antibiotics demonstrated greater effectiveness in alleviating symptoms and reducing disease severity in COPD patients compared to a focus on exacerbation management alone.

Keywords: COPD, CAT Score, mMRC Score, GOLD criteria, Methylxanthines, Corticosteroids, Antibiotics.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive disorder defined by persistent airflow limitation that is not totally reversible and is usually linked with an elevated chronic inflammatory response in the airways and lungs.[1] Common clinical manifestations include dyspnoea, chronic cough, sputum production, chest tightness, and recurrent exacerbations.[2,3] Tobacco smoking remains the predominant risk factor contributing to lung function decline and chronic inflammation in both current and former smokers with COPD.[3]

Globally, COPD was the fourth leading cause of mortality in 2004, accounting for 5.1% of deaths. In 2030, it is expected to account for 8.6% of fatalities, making it the third leading cause.[4] In India, the burden of COPD was particularly high, with an estimated 55.3 million cases reported in 2016, making it the second most common cause of mortality from non-communicable diseases (NCDs).[5] The prevalence of COPD among adults >35 years of age was reported as approximately 5% in men and 3.2% in women.[3]

To evaluate the health impact of COPD on patients' quality of life, the COPD Assessment Test (CAT) was developed as a simple, patient-completed questionnaire comprising eight items. Scores range from 0 to 40, with

*Corresponding author: Krishna Kumar Dhakchinamoorthi
Email: dr.dkrishnakumar@gmail.com

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higher scores indicating a greater impact of the disease: 0–10 (mild), 11–20 (moderate), 21–30 (severe), and 31–40 (very severe).[6,7] The modified Medical Research Council (mMRC) dyspnoea scale is also widely used to assess breathlessness, with scores ≥3 indicating severe breathlessness.[8]

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) initially classified disease severity based solely on airflow limitation (stages 1–4, from mild to very severe). However, the updated GOLD guidelines now recommend a more comprehensive ABCD assessment framework. This approach incorporates symptom severity (via CAT and/or mMRC scores) along with the patient's history of exacerbations in the preceding 12 months to guide clinical management.[9,10]

For hospitalized COPD patients, treatment guidelines recommend increasing the dose and frequency of bronchodilators. Systemic corticosteroids are advised for all patients, while antibiotics are reserved for those with clinical features suggestive of airway infections.[11] Commonly prescribed bronchodilators include beta-2 agonists, anticholinergics, and theophylline, which help relieve airflow obstruction during acute exacerbations (AECOPD).[12] In patients with moderate-to-severe COPD, triple inhaled therapy comprising an inhaled corticosteroid (ICS), a long-acting muscarinic antagonist (LAMA), and a long-acting beta-agonist (LABA) has demonstrated superior outcomes. This combination improves lung function, reduces symptoms, enhances quality of life, and lowers the risk of exacerbations and mortality compared to dual or monotherapy.[13,14] Additionally, combining short-acting muscarinic antagonists (e.g., ipratropium) with methylxanthines (e.g., theophylline) has demonstrated clinical benefits in the management of COPD.[15] The primary objective of our study is to further investigate and evaluate exacerbation control among COPD patients receiving methylxanthines, corticosteroids, and antibiotics, allowing for a three-way comparison (CAT, mMRC, GOLD) before and after therapy.

2. Materials and Methods

2.1. Study design and participants

This study was conducted in the inpatient department of Pulmonology at Government Medical College and Hospital, following approval from the Institutional Ethics Committee (EC/ME/2022, dated July 26, 2022). Over six months, a total of 120 patients of all genders, aged between 18 and 80 years, were enrolled. Eligible participants included individuals with a history of smoking or exposure to other COPD-inducing factors, who were admitted with complaints of productive cough and exertional dyspnea. Patients were excluded if they had any concurrent acute illness, were pregnant or lactating, or were unable to comprehend the study questionnaires. All the study participants provided written informed consent.

A comprehensive clinical history was taken, and symptom evaluation was conducted both before and after drug therapy using the COPD Assessment Test (CAT) and the modified Medical Research Council (mMRC) dyspnea scale. Additional data were collected using standardized questionnaires assessing the frequency of exacerbations and hospitalizations over the past year. Based on this information, patients were classified according to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria. Each of these scales were used according to standardized protocols to ensure the consistency and validity of data collection. GOLD classifications are used to determine initial treatment options for patients with COPD (**Figure 1**). Initial treatment followed GOLD-recommended first-line therapy for each group (A–D), but adjustments were made during follow-up based on clinical response. Patients with persistent dyspnea or frequent exacerbations despite initial therapy underwent stepwise escalation.

Those on monotherapy with a long-acting bronchodilator (LABA or LAMA) who continued to report high CAT scores or mMRC ≥2 were escalated to dual bronchodilation (LABA + LAMA). In cases of frequent exacerbations despite dual therapy, inhaled corticosteroids (ICS) were added, particularly in patients with high blood eosinophil counts. Short-acting bronchodilators were used for immediate symptom relief, and systemic corticosteroids or antibiotics were added temporarily during acute exacerbations. Treatment was regularly reviewed, and de-escalation was considered in patients experiencing adverse effects (e.g., ICS-induced pneumonia risk) or those who achieved stable symptom control. This titration strategy ensured a balance between efficacy, safety, and minimizing polypharmacy.

To evaluate the effectiveness of therapy in patients with COPD, both the CAT and mMRC scores were analyzed at baseline and post-treatment.

2.1.1. CAT score analysis

The CAT is an 8-item questionnaire assessing health-related quality of life in COPD patients. Each item is scored from 0 to 5, yielding a total score ranging from 0 (least severe) to 40 (most severe). In this study, a change of ≥2 points in the CAT score was considered clinically significant, based on established minimal clinically important difference (MCID) thresholds. [6] Post-therapy reductions in CAT scores were assessed both statistically and in terms of their clinical relevance using this threshold.

2.1.2. mMRC dyspnea scale analysis

The mMRC scale ranges from 0 (no breathlessness) to 4 (severe breathlessness limiting activity). A decrease of ≥1 grade in the mMRC score was considered clinically significant, consistent with GOLD guidelines.[1] Changes were evaluated to determine improvements in dyspnea severity and functional status following therapy. By applying these

MCID thresholds, the study ensured that observed score changes were not only statistically significant but also clinically relevant.

2.2 Statistical analysis

Statistical analyses were done using GraphPad Prism software. Results were expressed as mean ± standard deviation (SD) with 95% confidence intervals (CI). CAT scores, derived from an eight-item questionnaire evaluating the health status of COPD patients, and mMRC scores, based on interviews to assess the severity of dyspnea, were analyzed. The history of past-year exacerbations and hospital admissions was also considered. Using the data from CAT, mMRC, and exacerbation frequency, patients were categorized according to the GOLD classification. The CAT scores were compared using the Wilcoxon signed-rank test with continuity correction, and the Chi-square test of independence was used to compare the mMRC score. Changes in GOLD scores before and after therapy were assessed using a McNemar's test with continuity correction and a Chi-square test, with a p-value of <0.05 considered statistically significant. Similarly, the symptoms recorded before treatment were compared with those following administration of bronchodilators, corticosteroids, and antibiotics using a paired t-test, where $p < 0.05$ indicated statistical significance.

Comorbid conditions such as diabetes, hypertension, ischemic heart disease, and anemia are common in COPD and may influence symptom burden, therapy response, and functional status. However, the patients with concurrent illness were excluded from the study. Hence, adjustments were not made statistically for comorbidities in outcome analyses. The study compared pre- and post-treatment scores within the same patient to reduce intra-individual variation. However, no stratified or controlled analysis was done by the GOLD group or baseline CAT/mMRC category. Self-reported medication adherence was noted during follow-up visits, but not objectively quantified or adjusted for in statistical analysis.

2.2.1. Sample size/power analysis

To determine whether the sample size provided sufficient statistical power to detect a clinically significant change in outcomes, a post hoc power analysis was performed. Assuming a mean reduction of 4 points in the CAT score following therapy, with a standard deviation of 7 for the difference in pre- and post-treatment scores, the calculated effect size (Cohen's d) was approximately 0.57. Using a paired t-test with a significance level (α) of 0.05, the power of the study to detect this effect with 120 participants was estimated to be over 95%. This indicates a high probability of identifying a true treatment effect, if one exists. A similar calculation using the mMRC scores, assuming a mean reduction of 1 point with a standard deviation of 1.5, also yielded a power exceeding 90%. These findings suggest that the study was adequately powered to detect clinically significant changes in symptom burden and dyspnea severity following treatment, thereby enhancing the reliability and validity of the observed outcomes. However, future analyses may benefit from additional stratification or multivariable adjustment to further account for confounding variables.

3. Results

In this cross-sectional study, 120 patients' data were included for analysis. The mean age of the COPD patients was 58.5± 9.7 (mean± SD). The demographic details showed that a higher male patient ratio was included in the study cohort (**Table 1**). Among them, 70% were male and 3% were female, who had a history of smoking. Most of the patients presented with the symptoms of breathlessness (n=115; 95.8%), of which only (n=24; 20%) had the combination of breathlessness with expectorant.

CAT & mMRC scores revealed significant differences ($p < 0.0001$) between the day of admission and post-therapy (**Table 2**). A statistically significant reduction in COPD symptoms was observed after treatment, as measured by the COPD Assessment Test (CAT) score. The median CAT score decreased from 24 before treatment to 18 after treatment, while the mean score dropped from 23.97 to 17.13. This difference was statistically significant according to the Wilcoxon signed-rank test with continuity correction ($V = 7021$, $p < 0.001$). A statistically significant improvement in dyspnea severity was observed following treatment, as assessed using the modified Medical Research Council (mMRC) dyspnea scale. Before therapy, the majority of patients were classified as Grade 3 (56%) or Grade 4 (9%), indicating more severe breathlessness. Post-treatment, there was a marked shift toward lower grades, with 41% of patients reporting Grade 1 dyspnea, 51% reporting Grade 2, and only 4% remaining at Grade 3. No patients remained in Grade 4. A Chi-square test of independence demonstrated that this change in grade distribution was statistically significant ($\chi^2 = 121.89$, $df = 4$, $p < 0.001$), indicating a substantial reduction in symptom severity after therapy (**Table 2**). The history of the number of exacerbation episodes and hospitalizations in the preceding one year (**Table 1**) shows that most of the patients had exacerbations twice (39%). However, the mean exacerbation was found to be 1.6± 0.9 (mean±SD). The mean history of hospitalization was found to be 1.26± 0.8 (mean±SD) days.

The patients were classified according to the GOLD criteria. Before initiation of therapy, most of the patients are in the GOLD class C (85%), followed by the GOLD class D (10%) and GOLD class B (n=6, 5%). After therapy, the patients are classified and shifted to GOLD class C to GOLD class B (92%), followed by GOLD class A (6%). There was a significant difference observed when comparing the GOLD class grade before and after therapy (**Table 2**). To statistically evaluate the most prominent change in GOLD

classification following treatment—specifically the shift from Class C to Class B—we applied McNemar's test with continuity correction to account for sparse and unidirectional data. The analysis revealed a highly significant transition of patients from Class C to Class B. The test yielded a chi-square statistic (χ^2) of 97.09 with a p-value < 0.001, indicating a substantial improvement in patient classification post-treatment.

Bronchodilators are the most prescribed drug in combination with antibiotics and corticosteroids (**Table 3**). Deriphylline, which is a combination of etophylline and theophylline, is most prescribed (82%) than other methylxanthines, followed by dexamethasone. Among prescribed antibiotics, cephalosporins were highly prescribed (**Table 3**). The majority of the patients were treated with methylxanthines of deriphylline in GOLD class B. Whereas deriphylline and aminophylline are used in GOLD class C and GOLD class D. Patients in the GOLD class B were not treated with corticosteroids; the majority of GOLD class C patients received SCS (80%), and GOLD class D received a combination of SCS + ICS. Cephalosporins and macrolides are commonly prescribed in GOLD class B and GOLD class C. Macrolides, cephalosporins, tetracycline, and penicillin were used in GOLD class D. Bronchodilators of SABA were used to treat GOLD class B and C. Dual therapy was prescribed as a combination of SABA + SAMA, LABA + SAMA, and SABA + LABA + SAMA were used in GOLD class D patients.

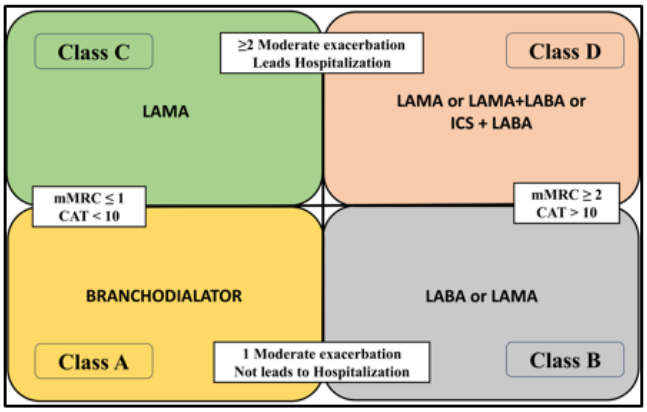

Figure 1: Therapeutic management of COPD based on GOLD criteria

This **Figure 1** represents the GOLD (Global Initiative for Chronic Obstructive Lung Disease) classification system for COPD, integrating symptom burden (assessed by mMRC and CAT scores) and exacerbation risk to guide initial pharmacologic therapy. Patients are categorized into four groups (A–D): Class A and B represent lower risk, with treatment options including bronchodilators or LABA/LAMA, while Class C and D indicate higher risk, requiring LAMA, combination inhalers (LAMA+LABA), or ICS+LABA depending on symptom severity and exacerbation frequency.

Table 1: Characteristics of the study population (n=120).

Characteristics	All patients n(%)	95% confidence interval
Age groups		
35 – 45 years	11 (9%)	0.05 – 0.15
46 – 60 years	59 (49%)	0.40 – 0.58
61 – 70 years	36 (30%)	0.22 – 0.38
71 – 85 years	14 (12%)	0.07 – 0.18
Gender		
Male	87 (73%)	0.63-0.79
Female	33 (27%)	0.20-0.36
Chronic smoker		
Male	84 (70%)	0.61-0.77
Female	3 (3%)	0.008-0.07
Biomass fuel exposure		
Male	-	
Female	33 (27.5%)	0.20-0.36
Symptoms present before therapy		
Male	87 (73%)	0.63-0.79
Female	33 (27%)	0.20-0.36
Symptoms present after therapy		
Male	21 (18%)	0.11-0.25
Female	4 (3%)	0.01-0.08
Symptoms before therapy		
Cough with expectoration	5 (4%)	0.01-0.09
Breathlessness and cough with expectoration	24 (20%)	0.13-0.28
Breathlessness	36 (30%)	0.22-0.38

Breathlessness and fever	21 (18%)	0.11-0.25
Breathlessness, cough, chest tightness	34 (28%)	0.21-0.30
Symptoms after therapy		
Cough with expectoration	18 (15%)	0.09-0.22
Breathlessness	4 (3%)	0.01-0.08
Breathlessness and cough	3 (3%)	0.008-0.07
Number of episodes of exacerbations ≤ 1 year		
No exacerbation	16 (13%)	0.08-0.20
1-time exacerbation	39 (33%)	0.24-0.41
2-time exacerbation	47 (39%)	0.30-0.48
3-time exacerbation	15 (13%)	0.07-0.19
4-time exacerbation	3 (2%)	0.08-0.07
Number of hospitalizations ≤ 1 year		
No hospitalization	22 (18%)	0.12-0.26
1-time hospitalization	56 (46%)	0.37-0.55
2-time hospitalization	32 (27%)	0.19-0.35
3-time hospitalization	8 (7%)	0.03-0.12
4-time hospitalization	2(2%)	0.04-0.05

Table 2: Baseline clinical and demographic characteristics of COPD patients before and after therapy (n=120).

Score/Classification	Before therapy (n=120) (%)	Mean	SD	After therapy (n=120) (%)	Mean	SD	*p*-value
CAT score[a]							
Score 1-10	-			7 (6%)			
Score 11-20	10 (8%)			108 (90%)			
Score 21-30	103 (86%)			5 (4%)			
Score 31-40	7 (6%)	23.93	3.14	-	17.20	2.67	< 0.0001
mMRC score[b]							
Grade 0	-			5 (4%)			
Grade 1	-			49 (41%)			
Grade 2	42 (35%)			61 (51%)			
Grade 3	67 (56%)			5 (4%)			
Grade 4	11 (9%)	2.75	0.61	-	1.57	0.64	<0.0001
GOLD score[c]							
Class A	-			6 (5%)			
Class B	6 (5%)			110 (92%)			
Class C	102 (85%)			4 (3%)			
Class D	12 (10%)	3.08	0.35	-	1.98	0.03	< 0.0001

CAT – COPD Assessment Test, mMRC – modified Medical Research Council, GOLD – Global Initiative for Chronic Obstructive Lung Disease

[a] Compared using the Wilcoxon signed-rank test with continuity correction

[b] Compared using the Chi-square test of independence

[c] Compared using a McNemar's test with continuity correction and a Chi-square test

Table 3: Therapeutic agents used to treat COPD based on GOLD classes (n=120)

Drugs	GOLD class B (n=6) (%)	GOLD class C (n=102) (%)	GOLD class D (n=12) (%)
Methylxanthines			
Deriphylline	6(5%)	96(80%)	-
Theophylline	-	4(3%)	2(2%)
Aminophylline	-	2(2%)	10(8%)
Corticosteroids			
SCS	-	96(80%)	-
ICS	-	2(2%)	-
SCS + ICS	-	-	12(10%)

Antibiotics			
Cephalosporins	3 (3%)	44(37%)	-
Macrolide	3(3%)	-	-
Amino penicillin	-	6(5%)	-
Cephalosporins + Macrolide	-	50(42%)	-
Cephalosporins + Tetracycline	-	-	4(3%)
Aminopenicillin + Macrolide	-	2(2%)	3(3%)
Cephalosporins + Tetracycline + Macrolide	-	-	2(2%)
Cephalosporins + Aminopenicillin + Macrolide	-	-	3(3%)
Other Bronchodilators			
SABA	2(2%)	100(83%)	4(3%)
SABA + SAMA	-	-	6(5%)
LABA + SAMA	-	-	1(1%)
SABA + LABA + SAMA	-	-	1(1%)
No medication	4(3%)	2(2%)	-

SCS – Systemic corticosteroids, ICS – Inhaled corticosteroids, SABA – Short-Acting Beta 2 Agonist, SAMA – Short-Acting Muscarinic Antagonist, LABA – Long-Acting Beta 2 Agonist.

4. Discussion

This cross-sectional study evaluated the demographic and clinical characteristics, symptom profiles, and therapeutic patterns in patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD). The study offers important insights into the impact of pharmacological therapy on disease severity and symptom control, as reflected by significant improvements in CAT and mMRC scores, and reclassification in GOLD stages. The mean age of the study population was 58.5 years, which aligns with the typical age range observed in COPD cohorts. The study population was predominantly male (73%), with a significant smoking history (70%), consistent with global evidence that smoking remains the principal risk factor for COPD in men.[1] Notably, among females, 27.5% had a history of biomass fuel exposure—a well-documented but often under-recognized risk factor, particularly in low- and middle-income countries.[16]

Clinically, breathlessness was the most common presenting symptom (95.8%), with 20% reporting concurrent expectoration. Post-therapy, this symptom burden markedly declined, indicating effective symptom management. The significant reduction in CAT and mMRC scores ($p < 0.0001$) further reinforces the effectiveness of the treatment regimens. Most patients initially had high CAT scores (21–30), but 90% improved to a moderate level (11–20) post-therapy. Similarly, mMRC scores shifted from Grade 3 to Grade 2 and Grade 1, reflecting improved functional status and dyspnea control. It demonstrates the clinical effectiveness of the treatment regimens. These findings are consistent with literature showing that optimized pharmacotherapy leads to symptom relief, improved exercise tolerance, and enhanced quality of life.[6,17]

Spirometry remains the cornerstone for the diagnosis and classification of Chronic Obstructive Pulmonary Disease (COPD), particularly through measurements such as FEV_1 (Forced Expiratory Volume in one second), FVC (Forced Vital Capacity), and the FEV_1/FVC ratio. According to the GOLD 2024 guidelines, a post-bronchodilator FEV_1/FVC ratio of <0.70 confirms persistent airflow limitation, which is characteristic of COPD.[1] Furthermore, newer studies have explored the role of serial spirometry in monitoring therapy response. A 2023 meta-analysis by Lee et al. found that improvements in FEV_1 over 6–12 months were modest but significantly greater in patients receiving combination bronchodilator therapy compared to monotherapy.[18] However, in the present study, lung function parameters (like FEV_1) were not included, which limits correlation with GOLD spirometric staging.

The GOLD classification changes post-therapy were particularly noteworthy. Before treatment, a majority were classified as GOLD C (85%), indicative of high symptom burden and exacerbation risk. Post-treatment, the majority were reclassified to GOLD B (92%), suggesting significant clinical improvement and reduced exacerbation risk. This finding underscores the value of appropriate pharmacological interventions in altering disease trajectory. The analysis of exacerbation and hospitalization frequencies revealed a substantial burden, with the average exacerbation rate of 1.6 per year and a hospitalization mean of 1.26. This highlights the importance of early intervention and optimized therapy to prevent acute events and reduce healthcare utilization.

Regarding pharmacotherapy, the frequent use of methylxanthines, especially deriphylline, reflects regional prescribing habits. Although methylxanthines are no longer first-line globally due to their narrow therapeutic index, they continue to be used in many settings due to cost-effectiveness and accessibility.[19] The extensive use of systemic corticosteroids (SCS) and inhaled corticosteroids (ICS) in GOLD C and D patients aligns with GOLD recommendations for patients with frequent exacerbations.[20] The combined use of cephalosporins and macrolides was common, likely reflecting bacterial involvement during exacerbations, consistent with previous studies highlighting bacterial infections as a frequent trigger.[21] Notably, dual and triple

bronchodilator therapies (SABA, SAMA, LABA combinations) were utilized predominantly in GOLD D patients, aligning with guideline recommendations for those with frequent exacerbations and higher symptom loads.[1,13,22] One strength of this study is the real-world data captured on symptom burden and response to therapy in a defined cohort. However, the study's cross-sectional design limits causal inference. Additionally, the absence of long-term follow-up restricts the evaluation of sustained therapy benefits. Potential confounders such as comorbidities or adherence to therapy were not assessed.

5. Conclusion

This study underscores the importance of tailored pharmacological therapy in improving symptom burden and reducing disease severity in COPD patients. The significant improvement in CAT and mMRC scores, along with favorable shifts in GOLD classification, supports the current therapeutic approaches. The findings also reflect the continuing use of traditional therapies like methylxanthines, highlighting the importance of context-specific treatment strategies in resource-limited settings. However, further longitudinal studies are warranted to assess long-term outcomes and optimize treatment algorithms in diverse COPD populations.

6. Source of Funding

None.

7. Conflict of Interest

None.

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