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Research Article

Unveiling the Clinical Profiles and Characteristics for Patients Starting Single-Inhaler Triple Therapy with Fluticasone Furoate/Vilanterol/ Glycopyronnium (FF/Vi/GLY): Results from an Indian Drug Utilisation Study

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Abstract

Introduction: Obstructive Airway Diseases (OADs) are the leading cause of death among chronic respiratory diseases worldwide, highlighting the urgent need for novel therapies. The combination of fluticasone furoate/vilanterol/glycopyrronium (FF/VI/GLY), a once-daily single inhaler triple therapy (SITT), has been recently introduced in India. However, there is currently no published real-world data available either from India or globally on the utilization of this novel regimen. Given the limited clinical experience with FF/VI/GLY in the Indian context, it is essential to systematically evaluate its real-world utilization, including its preference, prescribing patterns and clinical characteristics of patients.

Methodology: This retrospective, observational drug utilisation study at 360 outpatient clinics in India from July 2024 to December 2024. Prescription data and medical history of patients who were prescribed the FF/VI/GLY combination were collected. Ethics approval was obtained from an independent ethics committee prior to study initiation.

Results: FF/VI/GLY DPI was prescribed for COPD (49%), asthma (28.8%), and ACOS (20.8%). A total of 60.45% were switched from prior therapies-mainly ICS/LABA (35.03%) and LABA/LAMA (35.60%)-while 39.56% were treatment-naïve. Most COPD patients fell under GOLD Group E (53.7%) and Group B (36.4%), with a mean CAT score of 19.8 ± 8.1. Asthma patients were mainly in GINA Step 3 (33.6%) and Step 4 (26.5%), with a mean ACQ-5 score of 1.9 ± 1.2. Mean FEV_1% predicted was 45.65 ± 22.03%, with 61.87% of COPD patients showing very severe obstruction (GOLD 4). The average exacerbation rate was 2.2 per year; 68.8% of patients were hospitalized, and 41% had at least two exacerbation-related admissions. Common comorbidities included cardiovascular disease (40.9%), GERD (30.3%), and diabetes (29.7%).

Conclusion: This real-world study highlights a high symptom burden, frequent exacerbations, and severe airflow limitation in patients prescribed FF/VI/GLY DPI across India. The switch from prior therapies reflects a growing clinical preference for once-daily SITT in managing moderate-to-severe COPD, asthma, and ACOS, especially in multi-morbid patients.

Keywords: *Chronic Respiratory Diseases (CRDs); Obstructive Airway Diseases (OAD); Interstitial Lung Disease (ILD); Fluticasone Furoate/Vilanterol/Glycopyronnium (FF/Vi/GLY)*

Introduction

Chronic respiratory diseases (CRDs) encompass a range of lung conditions, including obstructive airway diseases (OAD), pneumoconiosis, interstitial lung disease (ILD), and pulmonary sarcoidosis. Globally, CRDs are amongst the leading cause of mortality, imposing a substantial healthcare and economic burden [1]. Among obstructive airway diseases (OADs), COPD and asthma are the most prevalent [2].

India bears a significant burden of COPD, with an estimated 37.8 million cases and over 9.5% of total national deaths attributed to the disease (GBD, 2019). COPD accounts for over 50% of the total CRD burden and 70% of disability-adjusted life years (DALYs) in India. Asthma also remains a major health concern, affecting 34.3 million individuals and contributing to disproportionately high morbidity and mortality [3].

India has a highly symptomatic and exacerbating COPD population, predominantly comprising GOLD groups B and E. Various Indian studies have reported the prevalence of Group B COPD ranging from 12.6% to 27%, while Group E COPD accounts for approximately 29% to 42% of cases. Patients with severe COPD exhibit high healthcare utilization, including frequent emergency visits, leading to considerable economic burden-particularly for those from lower-income groups. Delayed care-seeking due to low disease awareness and underreporting of exacerbations are common in real-world settings. Episodes of acute exacerbations of COPD (AECOPD) significantly impair lung function, quality of life, and physical activity [3].

Current GOLD guidelines recommend triple therapy for highly symptomatic patients and exacerbating group E patients [4]. The novel once-daily (OD) ICS/uLABA/uLAMA combination-Fluticasone Furoate/Vilanterol/Glycopyrronium (FF/VI/GLY) was approved in India in August 2023 [5]. Vilanterol (VI), an ultra-LABA, offers rapid onset, prolonged duration of action, and high β_2 receptor selectivity, reducing off-target cardiac effects. Fluticasone Furoate (FF), a highly potent ICS exhibits superior potency with lower systemic exposure compared to Fluticasone Propionate (FP). Glycopyrronium (GLY), a long-acting muscarinic antagonist (LAMA) is characterized by its rapid onset, prolonged duration, and high M3 receptor affinity, leading to improved lung function and enhanced symptom control [6].

Despite its clinical promise, real-world experience with FF/VI/GLY remains limited. This study seeks to address this gap by analysing prescription trends, baseline patient characteristics, comorbidities, and prior treatment histories of individuals and patient being initiated on this novel single inhaler triple therapy (SITT).

Materials and Methods

The present study was a multi-centric, observational, cross-sectional, drug utilization study conducted across 373 chest clinics in India over a six-month period, from July 2024 to December 2024, amongst chest physicians with at-least 10 Years of experience in managing OAD cases. Ethics committee approval was obtained from an independent ethics committee prior to study initiation (Good Society for Ethical Research). The requirement for informed consent was waived, as data were collected retrospectively and anonymized to ensure patient confidentiality. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The collected data included demographic details, history of exacerbations, medical history, hospitalizations in the preceding year, and clinical characteristics at the time of FF/VI/GLY prescription. Asthma severity was classified based on the Global Initiative for Asthma (GINA) 2024 guidelines, while COPD severity was categorized according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 criteria.

Patients prescribed FF/VI/GLY (100µg/25µg/50µg) via dry powder inhaler (DPI) with complete medical records were included in the study, while records with missing key data were excluded from the analysis. Symptom assessment tools included the COPD Assessment Test (CAT), the modified Medical Research Council (mMRC) dyspnea scale, and the Asthma Control Questionnaire-5 (ACQ-5).

The primary objective of the study was to evaluate the real-world utilization of FF/VI/GLY in outpatient departments (OPDs) of chest clinics across India. Secondary objectives included assessing FF/VI/GLY DPI use in relation to symptom scores, reliever medication use, medical history, and concomitant treatments.

All data were analysed using Microsoft Excel® (Microsoft Corporation, 2016, Redmond, USA), and descriptive statistics were generated

Results

Patient demographic and indication for FF/VI/GLY prescription

A total of 3730 patients' medical records were collected and analysed across 373 sites in India. The mean age of the study population was 52.4±12.5 years, with male predominance 71.3%. The primary indications for FF/VI/GLY DPI prescriptions were COPD (49%) and asthma (28.8%), with asthma-COPD overlap syndrome (ACOS) accounted for 20.8% of prescriptions. An additional 1% of cases included patients with symptoms such as cough, post-tuberculosis (TB) sequelae, and dyspnea, without a definitive diagnosis (Figure 1).

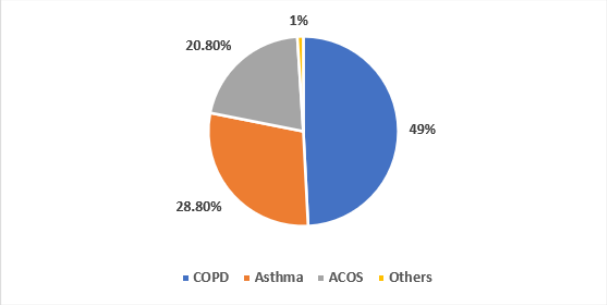

Figure 1: *Distribution of patients to whom FF/VI/GLY DPI was prescribed.*

Treatment history and switching patterns

In this study, 60.45% of patients were previously on other medications and were switched to FF/VI/GLY DPI, while 39.56% were treatment-naïve at the time of initiation. Among those who switched, prior therapies included mono, dual, or triple therapy. The most prevalent switch was from dual therapy, with 35.03% transitioning from ICS/LABA and 35.60% from LABA/LAMA. Additionally, 12.45% of patients were switched from other triple therapy regimens to once daily FF/VI/GLY DPI (Figure 2).

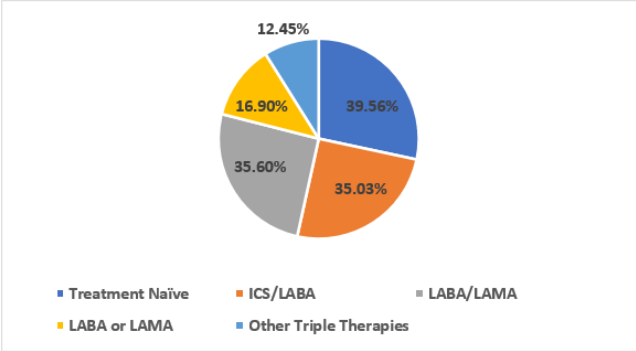

Figure 2: *Pattern of switching patients to FF/VI/GLY DPI.*

Disease severity and pulmonary function

In this study, the majority of COPD patients were under Group E (53.7%) and Group B (36.4%), while most asthma patients belonged to Step 3 (33.6%) and Step 4 (26.5%) of the GINA severity classification. The mean peak expiratory flow rate (PEFR) was 181.4 ± 154.1 L/min, with a mean predicted FEV1% of 45.65 ± 22.03%. Among the COPD patients, 61.87% had very severe airflow obstruction (GOLD Grade 4, FEV_1 <30% predicted), 21.66% had moderate obstruction (GOLD Grade 2, 50% ≤ FEV_1 <80%), and 10.11% had severe obstruction (GOLD Grade 3, 30% ≤ FEV_1 <50%) (Figure 3).

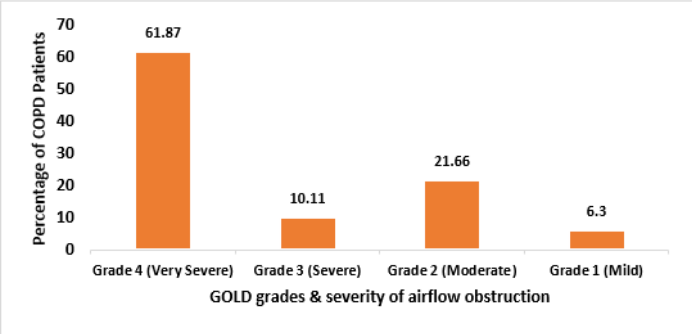

Figure 3: *Distribution of GOLD Grades and severity of obstruction.*

Symptom burden and disease control

Among COPD patients, the majority had mMRC Grade 3 dyspnea (41.19%), indicating breathlessness after walking 100 meters or within a few minutes, followed by Grade 2 dyspnea (29.97%) (Figure 4). The mean COPD Assessment Test (CAT) score was 19.8 ± 8.1, with 41.95% of patients scoring between 21-30 and 41.07% scoring between 11-20, reflecting a substantial symptom burden. For asthma patients, the mean Asthma Control Questionnaire-5 (ACQ-5) score was 1.9 ± 1.2, indicating uncontrolled asthma in a significant proportion of patients.

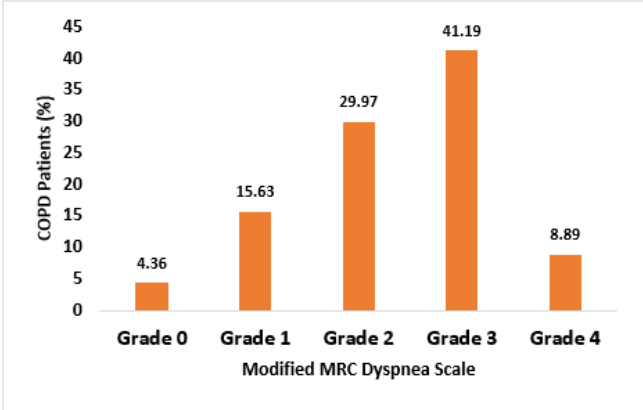

Figure 4: *Baseline mMRC score in patients switched to FF/VI/GLY DPI.*

COPD and Co-morbidities

The most prevalent comorbidities among patients were cardiovascular diseases (40.9%), gastroesophageal reflux disease (GERD) (30.3%), and diabetes mellitus (29.7%). In addition to these, several other less common comorbidities were observed, as illustrated in figure 5.

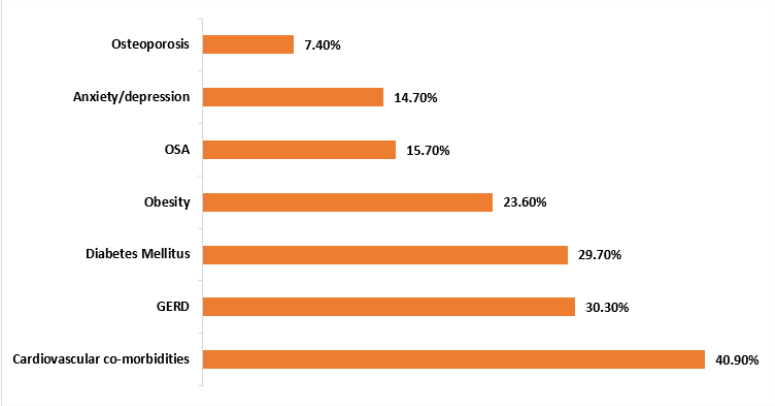

Figure 5: *Prevalence of co-morbidities in patients prescribed FF/VI/GLY DPI.*

Exacerbations history and hospitalisation

Analysis of exacerbation frequency over the past year showed that the mean number of exacerbations was 2.2, with a mean hospitalization rate of 1.3 due to exacerbations. A significant proportion of patients (58.62%) were classified as frequent exacerbators, with 28.10% experiencing two exacerbations, 10.95% experiencing three, and 19.56% reporting more than three exacerbations in the previous year. Among these patients, 68.80% had severe exacerbations requiring hospitalization, and 40.98% were hospitalized at least twice during the same period (Figure 6).

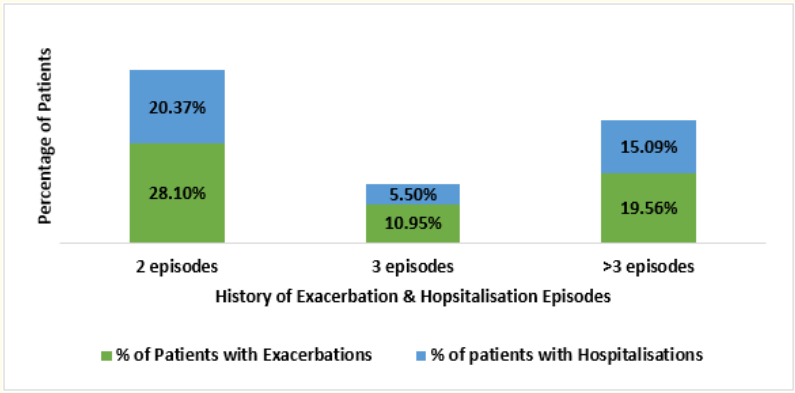

Figure 6: *Distribution of exacerbation and hospitalisation frequency in patients prescribed FF/VI/GLY DPI.*

Discussion

This study represents the first real-world evidence on FF/VI/GLY (VFG) from India, marking a significant milestone in the global landscape of single-inhaler triple therapy. This real-world drug utilization study not only provides insights for Indian clinicians but also serves as a reference model for emerging markets evaluating triple therapy innovations in OADs.

Various landmark clinical studies have shown that once-daily triple therapies have significantly improved lung function with enhanced symptom control, reduced exacerbations and mortality with improved adherence in OAD patients [3,7-9]. GOLD guideline recommends triple therapy for patients with persistent dyspnea, frequent exacerbations, or eosinophils ≥100 cells/μL [4]. Similarly, GINA also advocates for treatment escalation in asthma patients with poor control, especially those with type 2 inflammatory biomarkers (eosinophils ≥300 cells/μL, FeNO >50 ppb) [10].

COPD is marked by progressive lung function decline which tends to occur more rapidly in mild-to-moderate stages and in patients who smoke or experience frequent exacerbations. The recently published DEPICT-2 study emphasized the critical importance of timely pharmacotherapy showing that early initiation and escalation from dual bronchodilation to triple therapy in high-risk patients can help preserve lung function and improve quality of life [11]. This trend was reflected in our study, where 39.56% of patients initiated on FF/VI/GLY were treatment-naïve and 36.4% belonged to GOLD Group B. These findings suggest a shift toward earlier adoption of single-inhaler triple therapy, highlighting the evolving clinical confidence in initiating FF/VI/GLY earlier in the disease course.

A total of 56.5% of patients were escalated to FF/VI/GLY DPI, primarily from ICS/LABA (35.03%) and LABA/LAMA (35.60%), aligning with guidelines recommendation and also global clinical trial evidence-particularly IMPACT, ETHOS, and KRONOS-which demonstrated that triple therapy significantly improves lung function and reduces symptoms compared to dual therapy or multiple-inhaler regimens [12-14]. Moreover, earlier Indian data have shown widespread use of ICS in COPD patients [15] supporting the need for initiation of triple therapy in patients with high risk of symptom or patient with severe symptoms without exacerbation to prevent further risk of hospitalisation/exacerbations.

Exacerbation risk remains a critical factor driving treatment escalation. In this study, a considerable proportion of patients (58.62%) were identified as frequent exacerbators supporting the rationale for initiating triple therapy. Additionally, 71.98% of patients belonged to GOLD stages 3 and 4, indicating that FF/VI/GLY is being utilized in more severe and symptomatic individuals with a high disease burden.

Smoking-related damage extends beyond the lungs, significantly impacting the cardiovascular system, a concept that is now recognised by GOLD 2025 as syndemic occurrence [4]. Reduced pulmonary function is strongly associated with increased risks of congestive heart failure (CHF), myocardial infarction (MI), and atrial fibrillation (AF). A tertiary care study in India reported CVD comorbidities in 60% of COPD patients, underscoring their high prevalence [16].

The cardiovascular safety of bronchodilators is especially important in COPD patients with coexisting CVD. Vilanterol (VI), a highly β_2-selective ultra-LABA, provides prolonged bronchodilation with minimal cardiac effects [17]. The SUMMIT trial (16,000+ patients) confirmed the cardiovascular safety of FF/VI, showing no increase in CV events or mortality [18]. While LAMAs may affect cardiac rhythm via M2 blockade, glycopyrronium demonstrates high M3-over-M2 selectivity in preclinical studies and is associated with fewer systemic CV events than older LAMAs [19]. Our study reflected a multi-morbid COPD population, with FF/VI/GLY being prescribed in patients where nearly 95% had cardio-metabolic comorbidities. The favourable cardiac safety profiles of vilanterol and glycopyrronium may have influenced clinicians' preference for this combination in managing such high-risk patients.

The findings of this study reinforce the growing clinical preference for FF/VI/GLY DPI as a choice of SITT, particularly in patients with high symptom burden or uncontrolled symptoms despite dual therapies, patients with history of frequent exacerbations and patients with co-morbidities particularly cardiovascular or metabolic. The alignment of prescribing patterns with GOLD and GINA recommendations, combined with the pharmacological advantages of FF/VI/GLY, underscores its role as a clinically effective and well-tolerated option for moderate-to-severe COPD and asthma patients requiring treatment escalation.

This first-of-its-kind published study on FF/VI/GLY utilization in India provides valuable real-world insights into the patient populations and their characteristics receiving this therapy, addressing a critical gap in existing clinical evidence. However, the retrospective nature of the study and absence of longitudinal follow-up limit the assessment of long-term outcomes, treatment adherence, and disease progression. Further prospective and comparative studies-including head-to-head trials with other SITTs are warranted to confirm these findings and guide long-term treatment optimization strategies.

Conclusion

This first real-world study on FF/VI/GLY DPI utilization in India provides important insights into its use among patients with uncontrolled symptoms, frequent exacerbations, and comorbidities-particularly cardiovascular disease. The treatment patterns observed align with GOLD and GINA recommendations and reflect a shift toward earlier escalation based on clinical indicators and identifiable phenotypes. FF/VI/GLY emerges as a common SITT option in the management of moderate-to-severe obstructive airway making it more suitable for Indian practice, especially in patients with multiple comorbidities or low adherence potential.

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