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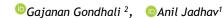
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Beliefs, experiences and behaviors during diagnosis and treatment of COPD in rural India: A large single center prospective, observational study of 6000 cases in tertiary care setting







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### **ABSTRACT**

Background: COPD (chronic obstructive pulmonary disease) is the leading cause of morbidity and mortality due to chronic respiratory illness in India. More than half of COPD patients were not getting adequate rationale inhalation treatment in primary to tertiary care setting.

Methods: Prospective, observational, interview (questionnaire) based complete workup COPD study conducted during June 2016 to June 2019 in Pulmonary medicine, Venkatesh chest hospital, & MIMSR Medical College, Latur screened 12000 cases with chronic respiratory symptoms with cough, sputum production and shortness of breath and all cases were undergone spirometry and 6000 COPD cases were enrolled. In this study we assessed disease knowledge, methods of treatment offered to all patients before enrollment by applying questionnaire. Statistical analysis was done using single proportion test (chi test).

Results: We have observed 3% study cases were aware about their illness 'COPD disease', 54% are not knowing the disease or not counseled for COPD disease ever before and 43 % cases are not convinced as they are having COPD (categorized as 'difficult patient') (p<0.0001). Inhalation treatment was offered in only 58% COPD cases, levosalbutamol monotherapy in 31% cases, levosalbutamol plus beclometasone in 18% cases, and formoterol plus budesonide or salmeterol plus fluticasone only in 9% COPD cases (p<0.0001), later being categorized as 'difficult treatment' being costlier than former ones. We also observed irrational and exuberant use of oral medicines in 42% COPD cases, theophylline in 16% cases, salbutamol in 7% cases, oral steroids in 19% cases and these medicines preferred by treating doctors over inhalation treatment in spite of knowledge of inhalation treatment and categorized as 'difficult doctor' (p<0.0001)

Conclusion: COPD is less efficiently evaluated and halfheartedly treated in rural setting, and more emphasis to be given to spirometry trainings for proper diagnosis and awareness regarding advantages of inhalation treatment over oral medicines.

Key words: COPD, spirometry, salmeterol fluticasone, difficult doctor, inhalation treatment

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the second leading cause of death in the world and affects an estimated 300 million people, while in India it is the second leading cause of death and affects an estimated 53 million people.<sup>[1]</sup> Chronic respiratory diseases commoner in India are COPD, Asthma, Bronchiectasis, interstitial lung diseases and posttuberculosis obstructive airways diseases, of which first two are more common to manifest similar clinical presentation with cough, shortness of breath and with or without sputum production. According to GOLD (global initiative for obstructive lung disease 2021 guidelines, Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[2] Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death worldwide, causing 3.23 million deaths in 2019. Over 80% of these deaths occurred in low- and middle-income countries (LMIC).[2] COPD includes chronic bronchitis, emphysema and small airway disease. chronic bronchitis is clinical definition, emphysema is radiological definition, and small airway disease is spirometry definition. Chronic bronchitis is defined clinically as the presence of a chronic productive cough for 3 months during each of 2 consecutive years (other causes of cough being excluded). Emphysema, is defined pathologically as an abnormal, permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis.

Although exact data of COPD disease prevalence, and its impact is not available due to diverse population and cultural trends here in India with 1.35 billion plus population, few published studies have documented prevalence of asthma and COPD in particular geographical setting in India. [3-5] The Burden of Obstructive Lung Disease Initiative Survey (BOLD) was one of the major data sources used to estimate COPD prevalence in India.

In 2017, the India State-Level Disease Burden Initiative reported varied epidemiological transition occurring among the states of India from 1990 to 2016 as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2016.<sup>[6]</sup> The National Health Policy of India 2017 recommends that premature mortality from non-communicable diseases, including chronic respiratory diseases, should be reduced by 25% by 2025.[7] COPD awareness has positive impact on disease diagnosis and rational treatment due to heterogenous trends of practices in country as varieties of pathies (Allopathy, Homeopathy, Ayurveda, Unani and others) are involved in treatment of these conditions.

Spirometry has vital role in diagnosis of COPD and is recommended by GOLD. Spirometry facility is not available in majority of centers in country with its limited use due to lack of awareness, although it is most cost-effective test to diagnose COPD. Spirometry is the goldstandard, guideline-recommended test for the diagnosis of obstructive airways diseases (OADs), including asthma and chronic obstructive pulmonary disease (COPD).[8] It also helps distinguish between the two diseases, offers a useful index of severity and prognosis and helps pharmacotherapy. [9,10] guide appropriate Although COPD is progressive respiratory illness with chronic symptoms, oral and inhaled treatment options are available to control symptom control and prevent disease progression. Inhalation treatment is helpful in controlling symptoms adequately over oral medicines and documented role in prevention of exacerbations over oral medicines. Various inhalers are available in India ranging from shortacting drugs salbutamol to long-acting salmeterol/formoterol with inhaled corticosteroids and tiotropium; former being cheaper and available in majority of government hospitals also while later being the costlier and not available in government hospitals. In this study, we have studied trends of COPD disease knowledge and rational treatment in tertiary care setting in peripheral parts of India. [11]

## **METHOD**

Prospective, observational, interview (questionnaire) based complete workup COPD study conducted during June 2016 to June 2019 in Pulmonary medicine, Venkatesh chest hospital, & MIMSR Medical College Latur after IRB approval and screened 12000 cases with chronic respiratory symptoms with cough, sputum production and shortness of breath lasted for more than 3 months and all cases were undergone spirometry. Finally, we enrolled 6000 COPD cases diagnosed by Spirometry. In this study we assessed disease knowledge, diagnosis, methods of treatment offered to all patients by applying questionnaire.

Inclusion criteria: all cases above 35-year age with chronic respiratory symptoms with cough, sputum production and shortness of breath lasted for more than 3 months

Exclusion criteria: cases with chronic respiratory symptoms having alternative diagnosis present or past history of tuberculosis, bronchiectasis, interstitial lung diseases and lung abnormality on chest radiograph documenting alternative diagnosis.

Respiratory questionnaire (RQCOPD) developed by expert group of teaching faculties of two institutes used during interview and assessment before spirometry: response to each of following question noted as yes, no and don't know

- 1. Are you having cough, sputum production and shortness of breath lasted for three months or more?
- 2. Are you having knowledge regarding your symptoms or illness causing it?
- 3. Are you aware of terminology of COPD, Asthma, or obstructive respiratory diseases?
- 4. Are you knowing risk factors of your illness?
  - 5. Are you current or past smoker?
- 6. Have you undergone any investigation for illness in past?
- 7. Have you undergone spirometry test in past?
- 8. Which treatment received for your illness, oral or inhalation?
- 9. Why oral treatment is preferred and inhalation treatment is not preferred?
- 10. Are you using oral medicines in spite of knowing pitfalls of treatment?
- 11. Are you unaware of benefits of inhalation treatment?

- 12. Why short acting inhalers are preferred over long-acting inhaler, preferred by doctors or yourself?
- 13. Is the cost factor driving your treatment options irrespective of knowing regarding benefits of long-acting inhalation over short acting inhalation or oral medicines?
- 14. Have you ever denied for inhalation treatment for your illness in spite of prescription from your treating doctor?
- 15. Is your treating doctor prescribing oral medicines in spite of knowing your illness over inhalation treatment?
- 16. Telephonically interview of treating family physician or primary health care facility provider has taken regarding knowledge of COPD disease, spirometry and ideas about oral and inhalation treatment in COPD.

Case definitions considered in this study formulated by expert group of teaching faculties in two tertiary care institutes are:

- 1. 'Difficult patient': considered as when patients are not convinced or not ready to accept COPD disease in spite of spirometry abnormalities suggestive of disease with symptoms.
- 2. 'Difficult doctor': considered as when primary treatment providers are not convinced or not ready to start inhalation treatment in COPD disease in spite of knowing benefits of it over other treatment options.
- 3. 'Difficult treatment': considered as when patients economic status is unable to take rational inhalation treatment in COPD in spite of prescription from health care expert and patient himself knowing advantages of it over other treatment options.

All cases were subjected to general and systemic physical examination with vital parameters recordings and routine investigations hematological workup as complete blood counts, blood sugar level, kidney functions and liver functions, electrocardiogram to rule out systemic abnormality, sputum examination and chest radiograph to rule out infective etiology in view of chronic respiratory symptoms and then spirometry analysis for confirmation of COPD diagnosis.

Spirometry procedure was carried out as per ATS/ERS task force recommendation standardization of lung function testing.[12] Subjects who were found to have post-bronchodilator FEV1 (Forced Expiratory Volume in first second)/FVC (Forced Vital Capacity) < 0.7 were taken up for final analysis as this value indicates the cut-off for diagnosis of obstructive airway disease according to GOLD guideline. Bronchodilator Reversibility (BDR) was defined as an improvement in FEV1 by at least 12% and 200 ml over pre-bronchodilator value. FEV1/FVC ≥0.7 were excluded as those patients had either a normal spirometry or a purely restrictive ventilatory abnormality. Also, the individuals who failed to fulfil acceptability and reproducibility criteria of spirometry were excluded. The statistical analysis was done using single proportion test (chi test). P value was considered significant if it was below 0.05 and highly significant in case if it was less than 0.001.

# **RESULTS**

In this study, 6000 COPD cases were enrolled, between age group 35-91 years of age; age above 55 years were 60% (3600/6000) and age below 55 were 40% (2400/6000). In gender distribution in study group. male population was 68.33 % (4100/6000) and females were 31.66% (1900/6000). Main symptoms in study group were shortness of breath in 84% cases, cough especially dry in 68% cases, sputum production in 61% cases and fatigability in 41% cases. Risk factor analysis, smoking in 14% cases, biomass fuel exposure in 54% cases and agricultural dust or work in dusty environment in 32% cases. We have observed 3% study cases were aware about their illness COPD disease, 54% are not having knowledge about disease and 43 % cases are not accepting the COPD diagnosis (p<0.0001) (Table 1).

**Table 1:** Analysis of awareness of COPD by respiratory questionnaire

COPD Cases awareness assessment	Number of cases (n=6000)	Percentage
Aware about Copd disease	180	3%
Not knowing disease	3240	54%
Not convinced for COPD diagnosis (difficult patients)	2580	43%

Inhalation treatment use was documented in 58% COPD cases, 31% cases levosalbutamol monotherapy, 18% cases levosalbutamol plus beclometasone, and 9% cases either formoterol plus budesonide or salmeterol plus fluticasone(p<0.0001) (Table 2).

Table 2 Inhalation treatment method use in COPD cases

Inhalation treatment	Percentage proportion in COPD group as whole		Percentage proportion in inhaler group Only	
Levosalbutamol monotherapy	1860	31%	1860	53.44%
Levosalbutamol Plus Beclometasone	1080	18%	1080	31.03%
Formoterol plus Budesonide/ Salmeterol plus Fluticasone with or without Tiotropium (difficult treatment)	540	9%	540	15.51%

Oral medicines use was documented in 42% COPD cases, 16 % cases theophylline, 7% cases salbutamol, and 19% cases oral steroids (p<0.0001) (Table 3) oral and inhalation treatments in 42% and 58% cases respectively (Table 4).

Table 3:Oral treatment method use in COPD cases

	Percentage		Percentage	
	proportion in		proportion in oral	
	COPD group as		group	
	whole		Only	
Theophylline	960	16%	960	38.09%
Salbutamol	420	7%	420	16.66%
Oral steroids	1140	19%	1140	45.23%

Table 4: Oral and inhalation treatment in COPD cases

	Number of cases (n=6000)	Percentage
Inhalation	3480	58%
Orals	2520	42%

We have observed only 9% cases received rational inhalation treatment (difficult treatment), 43% cases were not accepting the diagnosis (difficult patient) and in 42% cases were not offered rational treatment (difficult doctor)(Table 5).

**Table 5** Difficult doctor, difficult treatment, and difficult patient in study cases

	Number of COPD cases	Percentage
'Difficult patient'	2580/6000	43%
'Difficult treatment'	540/6000	9%
'Difficult doctor'	2520/6000	42%

### DISCUSSION

Prevalence of awareness of COPD in rural setting attending tertiary care hospital:

We have observed 3% cases were aware about their illness 'COPD', 54% are not knowing the disease at all or similar terminology till enrollment or never counseled for COPD disease ever before and 43 % cases

are not convinced as they are having COPD even after spirometry confirmation. (p<0.0001)

As our study was conducted in peripheral part of India with predominant rural background, with literacy rate above 60 percent with gender correction, COPD awareness is documented in 3% case only, we further asked how they come to know and they told us regarding acquired some knowledge about COPD form digital media. Similarly, Ghorpade et al [13] conducted study in urban slums and rural setting and documented awareness about COPD only in 1% population. Other studies have reported awareness rates of 49% in Turkey [14], 21% in Japan [15], 17% in Spain[16], 8% in France[17], 17% in Canada [18], 4% in Brazil [19], 10% in Germany [19], and 1% in Korea [19]. If we compare our data and published data by Ghorpade et al [13] with data of western countries, Indian rural population is least aware about COPD. Lack of knowledge, less awareness and minimal use of spirometry by family physicians are the reason for less awareness about COPD in community. We also observed majority of cases i.e., 54% cases were unaware of their lung disease as the reason for chronic symptoms and they were totally new to spirometry and COPD both and they were picked up too early if spirometry was used in early course by their family physicians. J. Zielinski et al [20] documented similar findings in their study and mentioned that 42% increase in COPD diagnosis with spirometry in symptomatic cases. Author Buffels et al. [21] analyzed the usefulness of spirometry performed by general practitioners in early diagnosis of COPD. We have observed that these cases have been missed and halfheartedly treated as spirometry is not available in peripheral setting. Proper trainings regarding methodology of spirometry are must as many of the cases will be missed due to faulty techniques of spirometry. Authors, Eaton et al. [22], Schermer et al. [23], and Enright et al. [24] documented similar observation and mentioned that proper training of spirometry is must to meet acceptability and reproducibility criteria. Mannino D M et al [25] mentioned that, in largest Population-based survey data from United States during 1991-1994 National Health and Nutrition Examination Survey (NHANES), less than half cases with COPD receive actual physician

diagnosis similar to our findings. Studies [26,27,28,29] have documented increased global prevalence of COPD due to increased tobacco consumption, which is equally associated with underdiagnosis and undertreatment.

Types of inhalation treatments prescribed to COPD in rural setting attending tertiary care hospital

Inhalation treatment was offered in only 58% COPD cases, levosalbutamol monotherapy in 31% cases, levosalbutamol plus beclometasone in 18% cases, and formoterol plus budesonide or salmeterol plus fluticasone only in 9% COPD cases (p<0.0001). Inhalation is the preferred administration route for COPD therapy due more targeted therapy with significant improvement in symptom control and lesser side effects due to smaller volume of drug required as compared to oral or intravenous route.[30] GOLD guidelines recommend to use inhalation therapy in combinations of long-acting bronchodilators with inhaled corticosteroids and or antimuscarinic agents as frontline therapy for COPD.[2] Similarly, various studies have documented COPD management remains suboptimal due to lack of knowledge or unaware regarding current guidelines to the management and poor adherence due less awareness in patients by treating physicians regarding rational inhalation treatment.[31,32] Foster et al [32] mentioned similar observations to our study, and primary care physicians prefer different choices of drugs during treatment of COPD, and especially keep note on preference of long acting beat agonist (salmeterol or formoterol) in 35 % cases of COPD which is very much higher to our study of 9% only. Authors in various studies [33,34,35,36] have documented cost factor is major driving factor during rational inhalation treatment and reason for underuse of long-acting beta-agonist combination with inhaled corticosteroids. Also, various authors [37,38,39] have observed additional use of tiotropium in COPD cases, and specifically documented cost factor for it use but it will decrease overall cost of treatment by decreasing hospitalizations. Indian guidelines also mention Inhalation treatment as rational therapy in management of COPD. [40]

Oral treatment prescribed to COPD in rural setting attending tertiary care hospital

We also observed irrational and exuberant use of oral medicines in 42% COPD cases, theophylline in

16% cases, salbutamol in 7% cases, oral steroids in 19% cases. (p<0.0001). Authors [41,42,43,44] have documented similar preferences and trends of use of oral medicines in these cases as it is cheaper one, easily available and simple to use and adequate symptom control with these medicines although long term benefits are not known or not expected by patients. GOLD guidelines [2] and Indian guidelines [40] recommended against use oral medicines in COPD unless patient is unaffordable and or inhaled medicines are not available.

Beliefs, experiences and behaviors observed during study as difficult treatment, difficult patient, difficult doctor

We have observed that 43% study cases diagnosed to have COPD after spirometry are not accepting the diagnosis and convinced for rational inhalation therapy recommended as per GOLD guidelines, and we called these cases as 'Difficult patients.' We further asked reasons for opting out inhalation treatment and preferring oral medicines are their misbelief as once it is started it has to continue to take for entire life without any gap, once inhalation started it will decrease lung strength, inhalation treatment will have adverse events on other organs of body including renal dysfunction; may be some patients experienced increased creatinine due to worsened obstructive uropathy with tiotropium use in benign prostatic hyperplasia, some believe this is last resort to control respiratory symptoms and it should be reserved and oral medicines should be tried first for disease, some believe that inhaled medicines will weaken respiratory tract and should be avoided as far as possible, some patients have experienced altered speech or dysphonia after inhalation use due to improper drug washout deposited in upper airways and feeling fear of loos of voice and stopped using it.

We have documented that formoterol plus budesonide or salmeterol plus fluticasone with or without tiotropium in 9% COPD cases only, and categorized as 'difficult treatment' being costlier and not pocket friendly than former ones. Most common misbelief is patients consider higher strength treatment being costlier to short acting bronchodilators and these medicines should be reserved during later course of illness

or when disease course advances, some patients also believe that these medicines may cause more systemic side effects. Patients experiences some relief with short acting drugs although not as much as long-acting drugs, they consider symptomatic relief as basic disease control parameter. As per our study, cost is the basic factor for least preference of long-acting drugs in management of COPD.

We also observed irrational and exuberant use of oral medicines in 42% COPD cases, and these medicines preferred by treating doctors over inhalation treatment in spite of knowledge of inhalation treatment and categorized as 'difficult doctor'. As per our study, most common reason for oral medicines preference is lack of knowledge regrading benefits of rational inhalation treatment, misbelief in correlation with patients as it has to continue without gap and continued for entire life and some general physicians believe that they have experienced lost to follow-up cases whenever they offered inhalation treatment and those patients received oral medicines showing adequate adherence irrespective of partial symptom control i.e., patients are demanding oral medicines over inhaled medicines and due to lack of knowledge they were experiencing difficulty in explaining benefits of these methods of treatment.

In Conclusion, 'Doctor-patient-drug discordance clubbed as 'difficult doctor, difficult patient, and difficult treatment' is very common issue observed during diagnosis and management of COPD in peripheral setting in India. We recommend to use spirometry test as a routine in all chronic respiratory symptom's patients for exact diagnosis of COPD, and more emphasis should be given for trainings of family physicians to spirometry. Oral medicines are commonly preferred treatments in COPD over universally accepted inhalation treatment due to misbeliefs, experiences and behaviors of patients and doctors. We recommend more awareness and sensitization regarding benefits of rational inhalation treatment in COPD, especially advantages of these of treatment in symptom control, improvement in quality of life and long-term disease related outcomes, and special emphasis on their role in decreasing hospitalization risk during exacerbation and overall cost of treatment.

### **Disclosures**

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Design- SP,GG,AJ; Materials - SP,GG,AJ; Data collection and/or processing - SP,GG,AJ; Analysis and/or interpretation SP,GG,AJ Writing - SP,GG,AJ Critical review - SP,GG,AJ.

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