ORIGINAL RESEARCH

Evaluation of adherence to new GOLD 2019 guideline, its impact on cost and survival prediction in Chronic Obstructive Pulmonary Disease patients

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ABSTRACT

Aims & Background: The prevalence of chronic obstructive pulmonary disease (COPD) is very high in India leading to increased morbidity and mortality. Pharmacotherapy for the same has been updated on a regular basis. The current study analyzed adherence to standard guidelines and any impact on healthcare expenditure as well as on survival prediction. Our study aims to evaluate adherence to GOLD 2019 guidelines. Also, analysis of survival prediction by BODE index along with the cost of therapy in COPD patients. **Materials and Methods:** A Prospective, observational study of 8 weeks was carried out on the patients visiting the Medicine department at a tertiary care teaching hospital who was diagnosed with COPD. COPD-diagnosed patients were recruited as per inclusion criteria. Demographic profile, drug therapy, adherence to the regimen, and direct cost of whole therapy were analyzed. For survival prediction BODE index was used. Data were assessed via IBM SPSS 25.0. **Results:** As per GOLD grading, out of 36 patient's majority (69.4%) were found in GOLD 2 which is a moderate category in COPD patients. The majority of patients showed adherence to levosalbutamol and ipratropium bromide (1.25mg, 500mg) drug combination by inhalational route. Considering adherence, 6 patients received treatment as per the new GOLD 2019 guideline whereas 30 patients were discordant. The majority of patients (44.4%) had to spend only about 101-200 INR for the treatment. In survival prediction, BODE 2 scores were found maximum with 23 (63.8%) in numbers. **Conclusion:** This study evaluated very low adherence to the new GOLD 2019 guideline with the low economic burden on COPD patients treated in the government setup. Also demonstrates the value of BODE index scoring. Efforts are required to improve adherence with the latest recommended guidelines to further reduce morbidity and mortality. Clinical significance: By implementing evidence-based guidelines, healthcare providers can improve patient outcomes, reduce healthcare costs, and improve the overall quality of care for patients with COPD.

Keywords: Adherence, BODE index, COPD, Economic burden, GOLD 2019 guideline.

INTRODUCTION

The approximate estimated prevalence of Chronic Obstructive Pulmonary Disease (COPD) is 6.5–7.7% in India. COPD is predicted to become the second leading cause of death by 2030 worldwide. According to the Global Burden of Disease study 1990-2016, second leading cause of death and disability-adjusted life-years (DALYs) was COPD in India.1 Although COPD is not fully reversible, it is a treatable & preventable disease. Findings of Indian studies highlight that air pollution is a leading risk factor for COPD than other risk factors like smoking, occupational exposure.1 As leading risk factor being little bit inescapable, proper treatment according to guideline can reduce burden of cost, morbidity as well as mortality in COPD patients.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is a guideline developed by international COPD experts for treatment and prevention of COPD. They developed consensus documents based on latest research and evidence.2 Recently GOLD 2019 revised report has been

published with combined treatment approach which can reduce frequency and severity of exacerbation of COPD.3 Evidence of several studies suggests that there is limited adherence to guideline for treatment.4 It is important to adhere to updated guideline with upcoming newer drug and delivery system for prevention of exacerbation and treatment of the same.

Treatment of COPD and associated comorbidities require many resources and frequent hospitalization. This may lead to much more cost burden to patients as well as health care system. New GOLD 2019 guideline, categorized in to four (A, B, C, D) treatment group, cost of therapy will increase as severity (group C, group D) of disease increases. As the disease is a progressive disease, life-long therapy is needed in majority which may increase economic burden. Several international studies have shown that increasing guideline adherence can have great impact on reducing direct and indirect cost of therapy.5 Newer pharmaceutical treatment options have been increased in last decade that can decrease exacerbation with cut short on cost of therapy.

Being a second leading cause of mortality, prediction of survival in COPD by BODE index is reliable method to apply.6 It is a unique scoring system which use different variables to find out all cause of mortality and morbidity in COPD patients. This multi scoring system gives prognostic information of COPD patients.

Our study evaluated the prescribing pattern and adherence to guideline which predicted to have impact on pharmacoeconomic burden in COPD patients. BODE index, being reliable method for predicting survival, we also tried to correlate adherence to guideline with BODE index in our government setup. Ultimately, our study aiming to assess adherence rate to GOLD 2019 guideline along with current scenario of management impacting on economic pattern as well as prediction of survival accordingly in COPD patients.

METHODS

The study was carried out after obtaining permission from the Institutional Ethics Committee. The approval of the HOD medicine & hospital superintendent was taken & written consent of the patients was obtained in their vernacular language. Moreover, the confidentiality of the data maintained. This prospective, observational study of 8 weeks and was carried out on the patients visiting the Medicine department at a tertiary care teaching hospital who were diagnosed with COPD. However, selection criteria were applied. Inclusion criteria of our subjects were patients of either gender, more than 18 years of age groups, all cases diagnosed with COPD, patients with acute exacerbations as well as stable COPD and all categories of COPD patients. Major exclusion criteria were subjects who fit in the inclusion criteria, but are not consciously willing to contribute in the study, any other type of respiratory diseases like bronchial asthma, Pneumonia, bronchiolitis etc., any type of lung cancer with COPD, any cardiovascular events along with COPD, any other miscellaneous diseases with COPD and pregnant women.Patient followed up until discharge.

Data of the patients diagnosed with COPD mentioned in inclusion criteria were taken. Basic data regarding demographic profile, clinical & medication data as well as diagnostic test & relevant test were collected. Adherence was checked according to updated new GOLD 2019 guideline.3 To minimize variability spirometry was performed after adequate dose of at least one short acting inhaled bronchodilator. Specific spirometric cut points were used by physician was evaluated. Then further assessment was followed as per comprehensive revised COPD assessment criteria. This criterion was evaluated on GOLD Grade 1, Grade 2, Grade 3, Grade 4 and symptoms assessment was carried on based on Group A, Group B, Group C, Group D. These two combined approaches were used for evaluation of adherence to guideline. COPD assessment was carried out by chart which has been given by 2019 updated GOLD 2019 guideline and combined approach was followed for COPD assessment.7 For assessment of symptoms, modified MRC dyspnoea scale questionnaires were used.8 Further for comprehensive assessment of symptoms, “COPD Assessment Test” (CAT) was used. This is 8-item uni-dimensional measure of health status impairment in COPD. Its applicability is worldwide, freely access and validated translations are available in wide range of languages. It has 0-40 score range and is documented in new updated GOLD 2019 guideline as well as well-known publications.9 According to group and severity assessment initial pharmacological treatment was followed. Investigator checked adherence to this treatment guideline. For Pharmacoeconomic evaluation data were collected in terms of diect Cost of drug use per person per month and total direct cost of illness for whole study duration. To predict survival, BODE index scoring system was used. Investigator has calculated the score for each and every case of COPD.10

STATISTICAL ANALYSIS

After generating the data of total number of patients reported at the Department of Medicine during the study period, data were entered into Microsoft excel 2013 and analyzed with statistical software IBM SPSS 25.11 The participant’s general and disease-related characteristics were analyzed with frequency and percentage. Paired t-test and Pearson correlation coefficient statistical test were carried for finding correlation between COPD assessment scoring.P value less than 0.05 will be considered as statistically significant.

RESULTS

Total number of patients recruited were 36. Most of the patients (n=35) were above 40 years old,

maximum (n= 15) between 50-60 age group. Only one patient was below 40 years. Predominantly male (81%) cases were higher than female (19%). Most of the patients were working at non-chemical exposure related occupation 24 (66.6%) compared to chemical exposed occupation 12 (33.4%). Majority of patients had breathlessness (n=30) and cough (n=33) as a symptom. Other had fever, weakness and chest pain. Some of the patients had past complain of pulmonary Koch's (n=2), Covid-19 pneumonia (n=7), Appendectomy (n=1), hernioplasty (n= 1) and diabetes type 2 (n= 2). Considering cause of COPD, 29 patients were had a habit of smoking and 6 were had large exposure of stove smoke.

Spirometry measurements used for COPD diagnosis. FVC (Forced vital capacity) in our study, all the patient's FVC value is less than normal, both pre and post bronchodilator suggesting an obstructed airway disease-COPD. FEV1 (Forced expired volume in one second) is influenced by the age, sex, height, and ethnicity, and is best considered as a percentage of the predicted normal value. It is often measured after the patient has taken bronchodilator, which opens the airways and the values are used to grade the severity of patient's disease. FEV1/FVC: FEV1 expressed as a percentage of the FVC, giving useful index of limitation of airways. In our study, pre bronchodilator, maximum patients (n=30) have FEV1/FVC ratio less than 70%, while 6 have it less than 70%. Post bronchodilator, 13 patients had ratio more than 70%, while 23 still have ratio less than 70%.

The comprehensive revised COPD assessment was carried out as per updated GOLD 2019 guideline. In the GOLD grading, out of 36 patients 25 were found in GOLD 2 which is a moderate category in COPD patients. Besides, 8, 2 and 1 no. of patients found in GOLD 3 (severe), GOLD 4 (very severe) and GOLD 1 (mild) grade respectively (Figure 1).

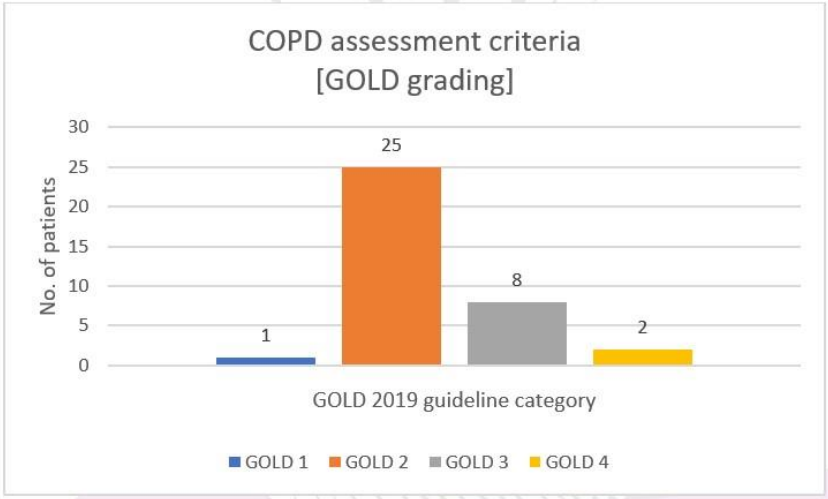

Figure 1: GOLD grading.

As per symptom-based grading in new guideline group wise distribution of patients has been depicted in figure 2.

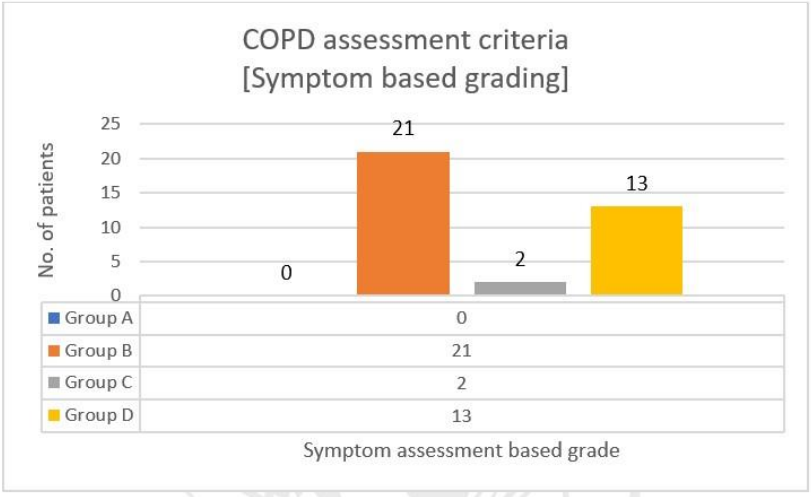

Figure 2: symptom based grading

Maximum 21 patients found in Group B followed by Group D (n=13) and Group C (n=2) showing majority were under "not leading to hospital admission" category. For COPD comprehensive assessment mMRCdyspnoea scale also evaluated which shows patients were categorized in grade 3 maximum 21 (58.3%) whereas no case was reported in grade 0. For measurement of health status impairment in COPD, COPD Assessment Test (CAT) was carried out and finding of that was shows there were nearly equal cases were under High impact CAT score (16, 44.4%) and Medium impact CAT score (15, 41.7%). mMRC Dyspnoea Scale score correlated with COPD assessment Test impact category shows significant correlation value which was 0.006 and Pearson Correlation was 0.448.

DRUG PRESCRIBING PATTERN

We analysed COPD guideline adherence as per COPD assessment and drug therapy management. Majority of patients were given levosalbutamol and ipratropium bromide (1.25mg, 500mg) drugs combination by inhalational route. Others drug use pattern were depicted in figure 3.

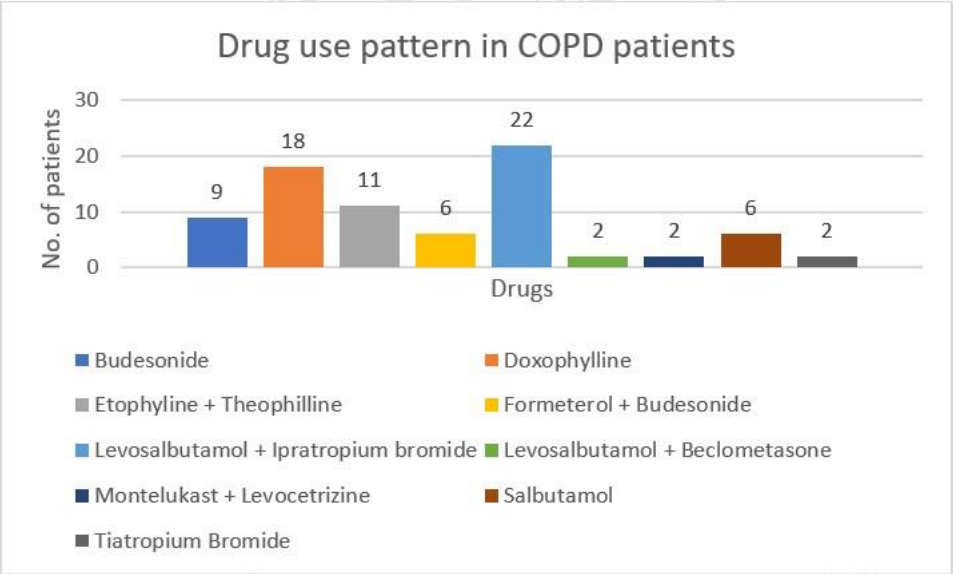

Figure 3: Drug use pattern in COPD patients

Large number of patients needed only twice daily inhalational puff. Main mode of drug delivery in all patients was inhalational drugs along with some oral drugs.

ADHERENCE TO GUIDELINE

Concordant & Discordant: 6 patients are concordant which means they are receiving treatment as per the GOLD 2019 guideline whereas 30 patients were discordant. As per GOLD group percentage of adherence has been shown in figure 4.

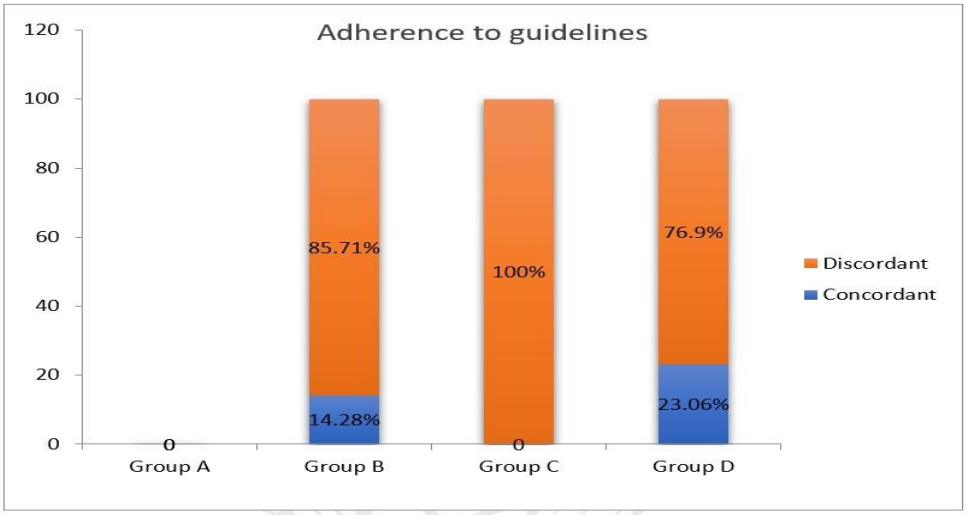

Figure 4: Adherence as per GOLD group

PHARMACOECONOMIC ANALYSIS

Figure 5 shows cost of drug per patient per month. Maximum patients (16) have to spend between 101-200 INR for the treatment. The treatment cost of 12 patients is between 201-300 INR. 4 patient's treatment cost is less than 100 and 4 need to spend more than 400 for treatment.

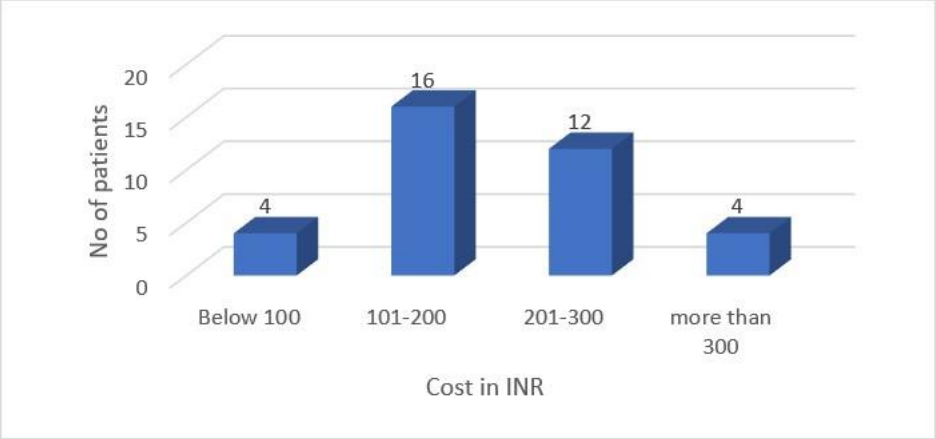

Figure 5: Patient's direct medical cost of treatment in INR

BODE INDEX ANALYSIS

BODE 2 score was found maximum with 23 (63.8%) in numbers. There were no cases in BODE 0 score (Figure 6).

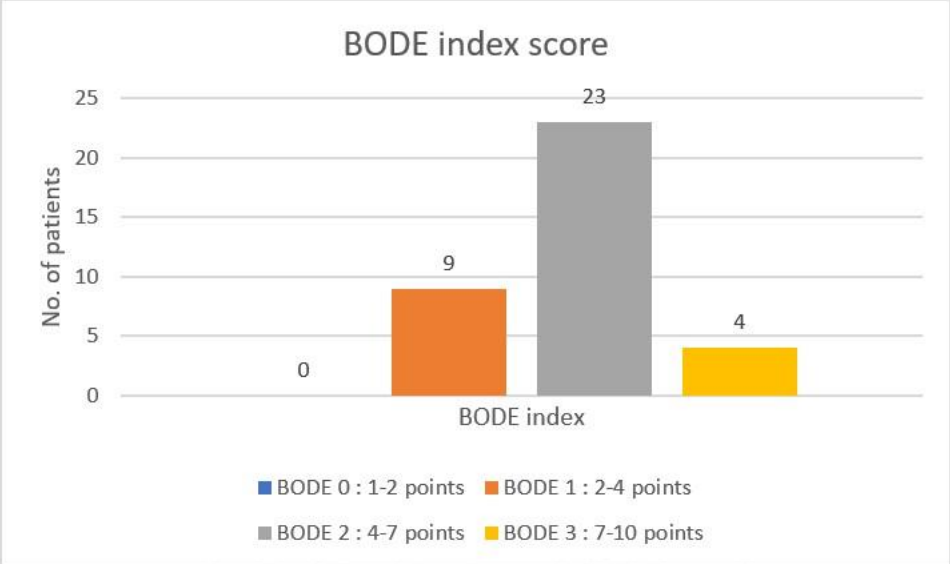

Figure 6: BODE index

DISCUSSION

Our study analyses adherence rate to new GOLD 2019 guideline, and its impact on cost and survival prediction by BODE index in Chronic Obstructive Pulmonary Disease patients. Out of 36 patients, most of the patients were in age group of 50-60 years. Prevalence of COPD between above 30 years of age was 1.6%-2.8%, according to study by Gudi et al12. The percentage change in death due to COPD was over 39% in India from 2007 to 201712. Majority of patients, in our study, had habit of smoking and some had exposure of smoke while cooking on stove emitting smoke. According to GOLD 2019 guideline, tobacco smoking, air pollution, occupational exposure are risk factors for COPD13.

For diagnosis of COPD, we used spirometry as it is considered to be gold standard for accurate measure of lung function. Post-bronchodilator ratio of FEV1 to Forced Vital Capacity of less than 0.7 is considered to be persistent airflow limitation according to GOLD 2019 guideline14. Less than 70% it indicates possible limitation of airways and the possibility of COPD. In

our study, one patient had FEV1 more than 80% showing mild COPD, 25 patients had FEV1 between 50 to 79% signifying moderate COPD. Eight patients had FEV1 between 30 to 49% signifying severe COPD, while 2 patients had severe COPD.

In our study, as per symptom-based grading according to new guideline, group wise distribution of patients, 58.33% patients were in Group B followed by 36.11% in Group D. Majority were under "not leading to hospital admission" category. These results are similar to results by Archipov14. Another similar study by Zbozinkova Z et al15 showed distribution of COPD patients as 30.6% GOLD B and 57% in GOLD D. 16.67% of patients were concordant which means they are receiving treatment as per the GOLD 2019 guideline whereas remaining 83.33% patients were discordant. This discordance maybe due to variability in availability of the drugs, it's cost and also may vary from doctor to doctor. Our findings are similar to findings by Parez et al16 in their study. Pharmacological discordance to guideline was also identified by Hsieh et al17. Clinical practice guideline is formed by systematic review of evidence, assessment of benefits and harms of alternative care options and they provide recommendations to optimize patient care18. Their main purpose is to improve effectiveness and quality of care and to decrease variations in clinical practice as well as to decrease expensive and preventable mistakes and adverse events. GOLD 2019 guideline is one such guideline. GOLD's goal was to increase awareness of COPD and thus prevent morbidity and mortality due to COPD. If GOLD 2019 guideline is used effectively, instances of un diagnosis of early stages of COPD can be prevented. In spite of benefits of GOLD 2019 guideline, many patients of COPD do not receive treatment as per GOLD 2019 guideline leading to poor prognosis and more economic burden over the period of time. There could be many barriers to non-adherence to GOLD 2019 guideline like poor familiarity and awareness with recommendations, low self-efficacy, time constraints etc. This information can be used to improve guideline adherence by administrators.

Management of COPD includes pharmacological as well as non-pharmacological therapy. Main purpose of pharmacological therapy is to reduce symptoms and severity of exacerbations to improve health of patients. Our study analysed COPD guideline adherence as per COPD assessment and drug therapy management. Majority of patients were given levosalbutamol (Short Acting Beta Agonist) and ipratropium bromide (Short Acting Muscarinic Antagonist) (1.25mg, 500mg) drugs combination by inhalational route. Large number of patients needed only twice daily inhalational puff. Main mode of drug delivery in all patients was inhalational drugs along with some oral drugs. Majority of patients were under treated which concordance with study done by Marmy JL et al study.19 Choice of treatment depends also on availability of medications, in addition to guideline's recommendations. Long-acting inhalers are recommended in majority of severe COPD patients, LAMA/LABA combination therapy is considered to be superior. Also, staging of COPD with spirometry (PFT) and adherence to GOLD 2019 guideline can reduce economic burden of the patients with moderate to severe COPD.20

In our study, 44.44% patients had to spend between 101-200 INR per month for the treatment, whereas for 33.33% patients, treatment cost was between 201-300 INR per month. Lakiang et al21 conducted a study to estimate direct and indirect costs of COPD. According to their study, mean yearly direct medical costs was Rs. 29,885 ± 11,995.33 and mean direct non-medical cost was Rs. 7,441.25 ± 2,228.90. These results differ from our study because ours being a government institute, drugs are freely available at free or low cost and most importantly group C & D patients were negligible. Another study conducted by Patel et al22 in Ahmedabad Gujarat also showed the mean direct medical costs for 6 months, related to COPD as Rs. 2,418.12 ± 839.73 and direct nonmedical costs as Rs. 528.01 ± 212.72. Also, the total direct cost of disease of COPD patients increased as duration of disease increased. Any comorbidity and the major complications also increased the costs of hospitalization and medication costs. As per Bhome et al23, the estimated burden of COPD for India was 35,000 crore INR in 2012. Appropriate use of LAMA plus LABA, LABA plus ICS, and LAMA plus LABA/ICS can reduce economic burden as well as can benefit the patient. It is essential to go for pharmacoeconomic evaluation of COPD to provide optimal therapy to patients at low price specially in private set up. As ours being a government set up and also limitation of study duration further more studies needed to strengthen the result of economic burden on COPD patients.

To predict long term outcome in COPD patients, BODE index was calculated. There were no cases in BODE 0 score. One-dimensional GOLD classification and multidimensional BODE index have similar clinical utility in predicting exacerbation in COPD patients24. In a study by Sarioglu et al25, 52% patients were in BODE 1 category, 21% patients were in BODE 2 category and there was significant relationship between BODE index and COPD stages classified according to GOLD 2019 guideline.

CONCLUSION

The study has highlighted the importance of implementing evidence-based guidelines for the management of COPD. Patient's adherence to new GOLD 2019 guideline was very low also reveal fact that economic burden of this disease in government setup was also low. Study found BODE index scoring is reliable tool for survival prediction. Overall, this study emphasizes the need for ongoing evaluation and implementation of evidence-based guidelines for the

management of COPD, in order to improve the quality of care and outcomes for patients with this condition.
Clinical significance: The clinical significance of this study lies in its potential to inform healthcare providers and policymakers about the importance of adherence to evidence-based guidelines in managing COPD, which can ultimately lead to improved outcomes for patients and a reduction in healthcare costs.

LIST OF ABBREVIATIONS

BODE: (Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity)
CAT:COPD Assessment Test
COPD: Chronic obstractive pulmonary disease
FEV1: Forced expiratory volume in 1 second
GOLD: Global initiative for chronic obstractive lung disease
LAMA: Long acting muscarinic antagonist
LABA: Long acting beta agonist
mMRC: Modified Medical research council

REFERENCES

1. India State-Level Disease Burden Initiative CRD Collaborators. The burden of chronic respiratory diseases and their heterogeneity across the states of India: The Global Burden of Disease Study 1990-2016. Lancet Glob Health. 2018 Dec; 6(12): e1363-e1374. doi: 10.1016/S2214-109X (18) 30409-1. Epub 2018 Sep 12.
2. Roisin RR, Rabe KF, Vestbo J, Vogelmeier C, Agustí A. On behalf of all previous and current members of the Science Committee and the Board of Directors of GOLD (goldcopd.org/committees/). European Respiratory Journal 2017 50: 1700671; DOI: 10.1183/13993003.00671-2017.
3. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2019 report. Last accessed January 16, 2020.
4. Sharif R, et al. Guideline adherence in management of stable chronic obstructive pulmonary disease. Respir Med. 2013;107(7):1046–1052. doi: 10.1016/j.rmed.2013.04.001.
5. Palmiotti GA, Lacedonia D, Liotino V etc. Adherence to GOLD 2019 guideline in real-life COPD management in the Puglia region of Italy. International Journal of Chronic Obstructive Pulmonary Disease. August 2018 Volume 2018:13 2455—2462. https://doi.org/10.2147/COPD. S157779.
6. Mapel DW, Roberts MH. New clinical insights into chronic obstructive pulmonary disease and their implications for pharmacoeconomic analyses. Pharmacoeconomics. 2012;30(10):869–885. doi:10.2165/11633330-000000000-00000.
7. Patel AR, Patel AR, Singh S, Singh S, Khawaja I. Global Initiative for Chronic Obstructive Lung Disease: The Changes Made. Cureus. 2019 Jun 24;11(6): e4985. doi: 10.7759/cureus.4985. PMID: 31453045; PMCID: PMC6701900.
8. Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllärniemi M, Saarto T. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. ERJ Open Res. 2017 Dec 14;3(4):00084-2017. doi: 10.1183/23120541.00084-2017. PMID: 29255720; PMCID: PMC5731772.
9. Ertan YE, Niksarlioglu EY, Yigitbas B, Bayraktaroglu M. How to Utilize CAT and mMRC Scores to Assess Symptom Status of Patients with COPD in Clinical Practice? Medeni Med J. 2022 Jun 23;37(2):173-179. doi: 10.4274/MMJ.galenos.2022.06787. PMID: 35735170; PMCID: PMC9234363.
10. Gökdeniz T, Kalaycıoğlu E, Boyacı F et al. The BODE index, a multidimensional grading system, reflects impairment of right ventricle functions in patients with chronic obstructive pulmonary disease: a speckle-tracking study. Respiration. 2014;88(3):223-33. doi: 10.1159/000365222.
11. IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.
12. Gudi, N., Mahmood, A., Roy, M. P., Ravishankar, Nayak, P., & Verma, A. (2021). Burden of COPD among population above 30 years in India: protocol for a systematic review and proposed meta-analysis. Canadian journal of respiratory therapy: CJRT = Revue canadienne de la therapierespiratoire : RCTR, 57, 14–17.
13. Alvar A, Decramer M, Frith P. Global initiative for chronic obstructive lung disease. Pocket guide to COPD diagnosis, management and prevention [Internet]. 2019.
14. Marçôa, R. et al. Classification of chronic obstructive pulmonary disease (COPD) according to the new global initiative for chronic obstructive lung disease (GOLD) 2017: comparison with GOLD 2011. COPD 15, 21–26 (2018).
15. Zbozinkova Z, Barczyk A, Tkacova R, et al. POPE study: rationale and methodology of a study to phenotype patients with COPD in Central and Eastern Europe. Int J Chron Obstruct Pulmon Dis. 2016;11:611–622.
16. Perez, X., Wisnivesky, J. P., Lurslurchachai, L., Kleinman, L. C., & Kronish, I. M. (2012). Barriers to adherence to COPD guideline among primary care providers. Respiratory medicine, 106(3), 374–381. https://doi.org/10.1016/j.rmed.2011.09.010.
17. HsiehMJ, HuangSY, YangTM, TaoCW, ChengSL, LeeCH, KuoPH, Wu YK, Chen NH, HsuWH, HsuJY, LinMS,WangCC, WeiYF, & TsaiYH (2018). The impact of 2011 and 2017 Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guideline on allocation and pharmacological management of patients with COPD in Taiwan: Taiwan Obstructive Lung Disease (TOLD) study. International journal of chronic obstructive pulmonary disease, 13, 2949–2959.
18. Faganello MM, Tanni SE, Sanchez FF, Pelegrino NR, Lucheta PA, Godoy I. BODE index and GOLD staging as predictors of 1-year exacerbation risk in chronic obstructive pulmonary disease. Am J Med Sci. 2010 Jan;339(1):10-4.17.
19. Marmy JL, Diedrich JP, Cadus C, Grendelmeier P, Tschacher A, Dieterle T, Chhajed PN & Leuppi JD. Adherence to GOLD Recommendations among Swiss Pulmonologists and General Practitioners, COPD: Journal of Chronic Obstructive Pulmonary Disease, 18:1, 9-15, DOI: 10.1080/15412555.2020.1859469.
20. Horita N, Goto A, Shibata Y, Ota E, Nakashima K, Nagai K, Kaneko T. Long-acting muscarinic antagonist (LAMA) plus long-acting beta-agonist (LABA) versus

LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2017 Feb 10;2(2):CD012066. doi: 10.1002/14651858.CD012066.pub2. PMID: 28185242; PMCID: PMC6464543.

21. Lakiang T., Nair NS., Ramaswamy A., & Singhal U. (2018). Economic impact of chronic obstructive pulmonary disease: A cross-sectional study at teaching hospital in South India. Journal of family medicine and primary care, 7(5), 1002–1006.
22. Patel KD, Lalwani T, Shah K. Economic burden in direct cost of Chronic Obstructive Pulmonary Disease at a tertiary care teaching hospital: A prospective observational cohort study. Indian J Pharm Pract. 2014;7:61–8.
23. Bhome A. B. (2012). COPD in India: Iceberg or volcano?. Journal of thoracic disease, 4(3), 298–309.
24. Li CL, Lin MH, Chen PS, Tsai YC, Shen LS, Kuo HC, Liu SF. Using the BODE Index and Comorbidities to Predict Health Utilization Resources in Chronic Obstructive Pulmonary Disease. Int J Chron Obstruct Pulmon Dis. 2020 Feb 19;15:389-395. doi: 10.2147/COPD.S234363. PMID: 32110007; PMCID: PMC7036670.
25. Sarioglu, N., Alpaydin, A. O., Coskun, A. S., Celik, P., Ozyurt, B. C., &Yorgancioglu, A. (2010). Relationship between BODE index, quality of life and inflammatory cytokines in COPD patients. Multidisciplinary respiratory medicine, 5(2), 84–91. https://doi.org/10.1186/2049-6958-5-2-84.