

Smoker Copd Patients Inquire Higher Medication Cost Than Non-Smoker Copd Patients: A 12 Month, Longitudinal, Pharmaco-Economic Analysis

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Abstract

A paucity of data in context to economic burden in COPD patients with and without history of smoking exists. The study evaluated the difference in medication expenditure in COPD patients with and without a history of smoking as an etiological factor. We screened 206 COPD patients treated at the department of respiratory medicine at Chettinad Hospital and Research Institute (CHRI), Kancheepuram, India, and enrolled 180 eligible patients, from August 2019 to July 2020. The baseline information collected during the initial visit includes demographics, smoking status, and respiratory medication regimens, and cost of medications (Inhaler, Oral and Parent Antibiotics and Glucocorticosteroids). Patients were further contacted during their hospital visit or by telephone to collect information on the ongoing treatment, at least 4 times during the study period. A total of 83 (53.20%) with smoking history and 73 (46.79%) without smoking history completed the study (n=156) with a mean age of 63.03 (SD ± 9.11). There was a significant difference in mean annual medication expenditure between non-smoker COPD cohort (INR 9089.74 \pm 4502.352) and smoker COPD cohort (INR 12234.82 \pm 6553.171), $p = 0.001$. The mean annual expenditure of inhaler medications, antibiotics, and glucocorticosteroids (oral and parental) was INR 8824.86 (SD \pm 3464.901), INR 1204.63 (SD \pm 1950.728), and INR 1415.52 (SD \pm 2687.040) in smoker COPD cohort and INR 7244.05 (SD \pm 1852.400), INR 542.60 (SD \pm 1288.121), and INR 686.63 (SD \pm 1861.491) in non-smoker COPD cohort respectively ($p = 0.000$; $p = 0.001$; $p = 0.007$). The current study verified that smoker COPD patients incurred significantly higher medication costs than non-smoker COPD patients reiterating the need to study COPD phenotypes further to optimize the treatment regimens.

Keywords: Chronic Obstructive Pulmonary Disease, Smoker, Medication Expenditure.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease characterized

by airflow limitation which is not completely reversible. A series of physiological changes influence the quality of life (QoL) and survival as the disease progresses. The burden of COPD

is estimated to be 210 million and globally it was the 4th largest cause of death and it is projected to be in the third position in 2030. India and China account for 66% of global COPD mortality. COPD was estimated to be 210 million and is projected to take the third position by 2030.^[1] The estimated deaths due to COPD were 500000/year and found to be in the range of 2-22% in men and 1.2 – 19% in women in different population studies.^[2] COPD is known to have a significant economic burden globally and COPD in the Indian population accounts for 4.8% of global disability-adjusted life-years (DALYs).^[3] The direct cost of medication in developed nations like the United States, China was reported to be \$29.5 and US\$30.30 billion annually.^[4] It is a different scenario in countries like India where most of the treatment cost remains to be out-of-pocket. Moreover, approximately 38% of the total healthcare cost is spent on medications alone in India which is much greater than the developed nations which are only 10%.^{[5], [6], [7], [8]} COPD patients in India spend more on medications than hospital charges.^[9]

Etiological factors exist beyond smoking as a cause for developing COPD. The 2017 Global Burden of Disease study has estimated that smoking accounts for only 35% of the global COPD burden, most of which occur in high-income countries.^[10] The remaining 65% of the non-smoking COPD burden occurs mostly in the low- and middle-income countries of the world. Exposure to biomass smoke during cooking in poorly ventilated homes, high levels of ambient air pollution, occupational exposures to dust and gases, ambient ozone exposure, poverty, repeated respiratory tract infections during childhood, poorly-controlled chronic persistent asthma, and previous tubercular lung disease is also non-smoking risk factors for COPD.^{[11], [12], [13], [14]} A wide range of studies published globally since 2005 shows the proportion of COPD patients who have never smoked ranging from 17% to 47.6%.^[15]

The cost associated with COPD was found to generally increase with poor adherence to the therapy and incorrect use of inhalers.^{[16], [17], [18], [19]} The COPD prognosis is co-related to

exacerbations and hospitalizations, both frequency, and severity and it directly influences the cost of treatment. The economic burden of COPD was studied both globally and in India but those were limited to the general COPD population with different severity levels. Although only a little known about non-smoker COPD patients, phenotypic differences have started to be examined, already. The financial impact of smoking on an individual was between 6 and 14% of health expenditure annually but its cost impact on COPD is inconclusive.^[20] Exacerbation frequencies, amelioration of dyspnea, mitigation of cough symptoms, and response to therapy during acute exacerbations were recorded to be better in non-smokers with COPD than those of smokers with COPD in few observational studies.^{[21], [22], [23]} There is still a need for a shred of concrete evidence to substantiate the differences between these different, evolving phenotypes on how they differ responding to treatment with bronchodilators, corticosteroids, antibiotics, and other supportive drugs. A better understanding of the utilization of health care services among COPD patients is also needed to assess the economic impact of interventions and improve the quality of care. In this study, we tried to evaluate the differences in the need and the cost of these medications between COPD patients with and without a history of smoking as an etiological factor.

MATERIALS AND METHODS

The study was carried out as part of a larger study evaluating the cost of medication used to treat COPD. The study was conducted at Chettinad Hospital and Research Institute (CHRI), a tertiary care teaching hospital in Kancheepuram, India, for over one year. Those with a confirmed diagnosis of COPD by the respiratory physician were selected and informed consent was collected before enrolling them into the study. The study has been reviewed and approved by the institutional ethics committee of Chettinad Hospital and Research Institute (CHRI), Kancheepuram, in accordance with the Declaration of Helsinki (525/IHEC/3- 19, Sep.2020).

Assessments

Treatment costs

At the time of patient recruitment, all patients were interviewed to collect baseline information. The cost of medications was collected based on the data available in the case record forms. The cost of medications includes the cost of oral and intravenous (IV) glucocorticosteroids, inhalers medications (bronchodilators, inhaled corticosteroids or fixed-dose combination of both), antibiotics. We excluded any medicines that were used to treat conditions other than COPD. The cost of the medications was collected at least during 4 timepoints (once in 3 months) during the fiscal year 2019–2020, in INR. The cost of the COPD medications use during hospitalizations was collected during the time of discharge.

The baseline information for each patient was collected during the first visit. The baseline information includes demographics, optimal inhaler use, smoking status, and respiratory medication regimens. Patients were further contacted during their hospital visit or by telephone to collect information on the ongoing treatment for subsequent months. Only patients who completed the entire study were included for final statistical analysis. The study design is mentioned in Fig. 1.

Data analysis

Data entered in Microsoft Excel. SPSS version 23.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analyses. Descriptive statistics calculated for baseline variables. Since the data did not follow the normal distribution, non-parametric tests of significance (Mann Whitney test and Kruskal Wallis test) were used to test the association between cost and another parameter.

RESULTS

A total of 206 COPD patients screened and 180 patients were found eligible to participate in the study. The final analysis was done with 156 patients who completed the study out of which 83 (53.20%) patients had a history of smoking and 73 (46.79%) did not. The mean age of the

COPD patients was 63.03 (SD ± 9.11). There were 90 (57.67%) male and 66 (42.3%) female COPD patients. A significant proportion (41.6) of patients were in the age group between 61 to 70 years. The mean duration of COPD (years since diagnosis of COPD) was 8.6 ± 3.4 in the overall study population. There were 22 (14.1%), 71 (45.5%), 50 (32.1%), and 13 (8.3%) found to be in the mild, moderate, severe, and very severe COPD categories among the study participants. The baseline characteristic was mentioned in Table I.

In the smoker COPD group, 63 (75.9%), 17 (20.5%), 3 (3.6%), 0 (0%) and in the never-smoker COPD group, 63 (86.3%), 8 (11.0%), 1 (1.4%), 1 (1.4%) of them were hospitalized 0, 1, 2 and 3 times in twelve months study period. Similarly, 34 (41.0%), 10 (12%), 20 (24.1%), 17 (20.5%), 1 (1.2%), 1 (1.2%) of never-smoker COPD patients and 48 (65.8%), 12 (16.4%), 11 (15.1%), 1 (1.4%), 0 (0%) and 1 (1.4%) of smoker COPD patients had 0, 1, 2, 3, 4, 5 exacerbations during the course of study period. Concerning the exacerbation and hospitalization frequency, difference between COPD patients with and without history of smoking was clearly established though statistical significance was achieved only for exacerbation frequency ($p=0.001$).

The study had witnessed a steep increase in medication expenditure in patients as the frequency of hospitalization and exacerbation increases irrespective of the smoking status. The cohort with no incident of hospitalization over the entire study period had reported spending INR 8501.09 ± 3372.908 and patients who were hospitalized once, twice, and thrice had spent INR 19462.92 ± 3138.087 , INR 27745.25 ± 2316.287 , INR 28103.00 ± 3215.09 for medications, annually. There was a strong correlation between the mean medication cost and the exacerbation frequency as displayed in Figure 2 (A and B).

The total mean medication expenditure for the entire twelve months in the non-smoker COPD cohort was INR 9089.74 ± 4502.352 and it was INR 12234.82 ± 6553.171 in the smoker COPD

cohort. (Figure 3) The difference between these two groups was statistically significant. ($p = 0.001$). On assessing the frequency of exacerbation, 13.8% of the non-smoker COPD group and 24.1% of the smoker COPD group were hospitalized at least once during the study period. At the same time, 25 non-smoker COPD patients and 49 smoker COPD patients experienced a minimum of one exacerbation. (Table II) The mean annual expenditure of inhaler medications, antibiotics, and

glucocorticosteroids (oral and parental) was INR 8824.86 (SD \pm 3464.901), INR 1204.63 (SD \pm 1950.728), and INR 1415.52 (SD \pm 2687.040), in smoker COPD cohort and INR 7244.05 (SD \pm 1852.400), INR 542.60 (SD \pm 1288.121), and INR 686.63 (SD \pm 1861.491) in non-smoker COPD cohort respectively. The mean monthly expenditure of inhaler medications, antibiotics, and glucocorticosteroids (oral and parental) was mentioned in Figure 4 (A-C).

Table I - Baseline Characteristics

Characteristics		N (%)
Age (Mean)		63.03 (SD \pm 9.11)
Sex	Male	66 (42.3%)
	Female	90 (57.67%)
Smoking History	Yes	83 (53.20%)
	No	73 (46.79%)
COPD Severity	Stage I (mild)	22 (14.1%)
	Stage II (moderate)	71 (45.5%)
	Stage III (severe)	50 (32.1%)
	Stage IV (very severe)	13 (8.3%)
Mean duration of COPD - (Years)		8.6 \pm 3.4

Table II - Frequency of Hospitalization and Exacerbation in COPD Patients with and without History of Smoking over 12 Month Study Period

Variables	COPD Patients without History of Smoking	%	COPD Patients with History of Smoking	%	P value
Hospitalization Frequency					
0	63	86.3%	63	75.9%	0.202
1	8	11.0%	17	20.5%	

2	1	1.4%	3	3.6%	
3	1	1.4%	0	0%	
Exacerbation Frequency					
0	48	65.8%	34	41.0%	0.001*
1	12	16.4%	10	12.0%	
2	11	15.1%	20	24.1%	
3	1	1.4%	17	20.5%	
4	0	0%	1	1.2%	
5	1	1.4%	1	1.2%	

* Statistically Significant

Fig. 1 Flow chart representing number of patients at different timepoint during the study

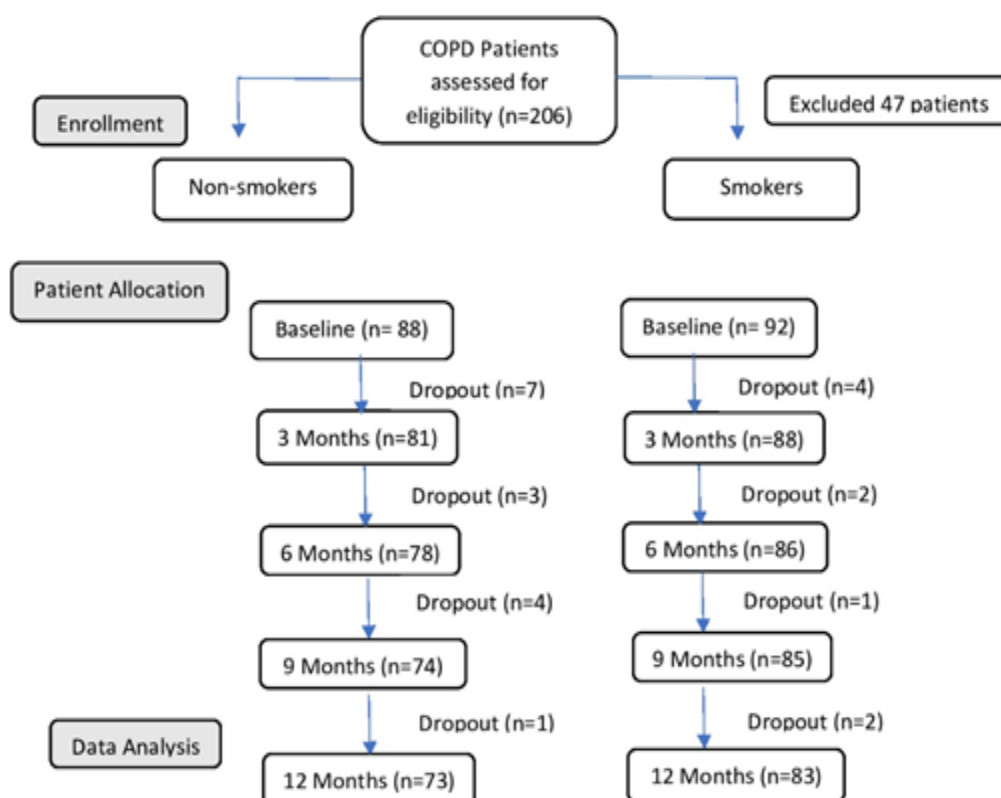


Figure 2. Total annual medication expenditure in COPD Patients based on Hospitalization (A) and Exacerbation (B) Frequency

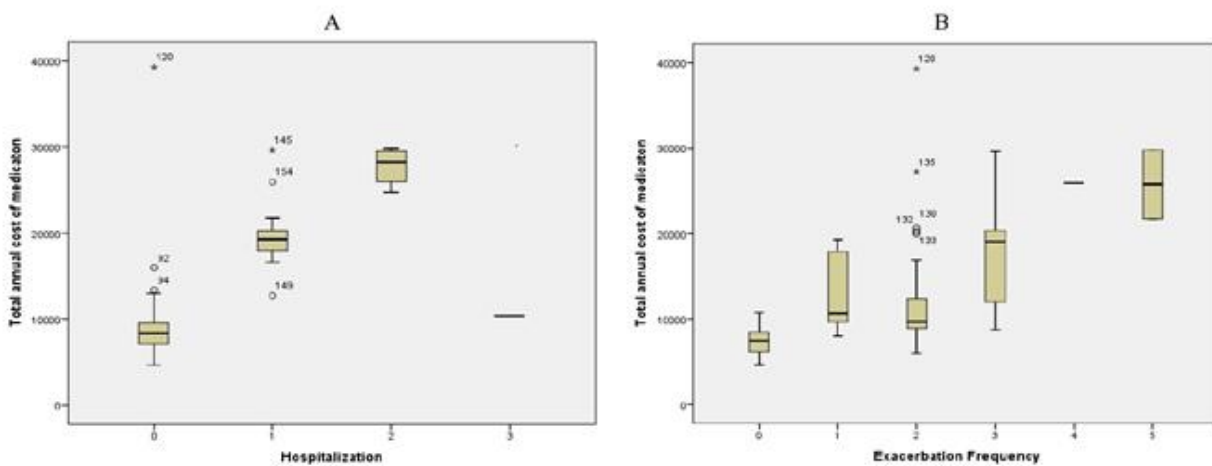


Figure 3. Comparison of annual medication expenditure in Smoker and Non-smoker COPD patients

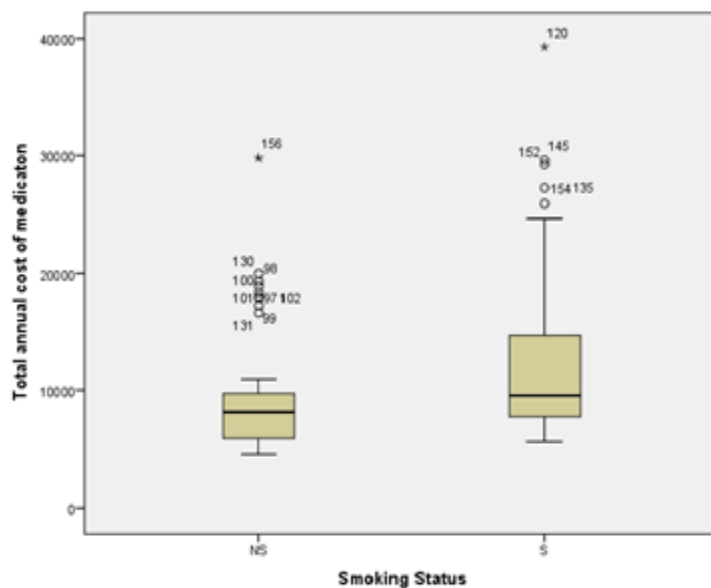
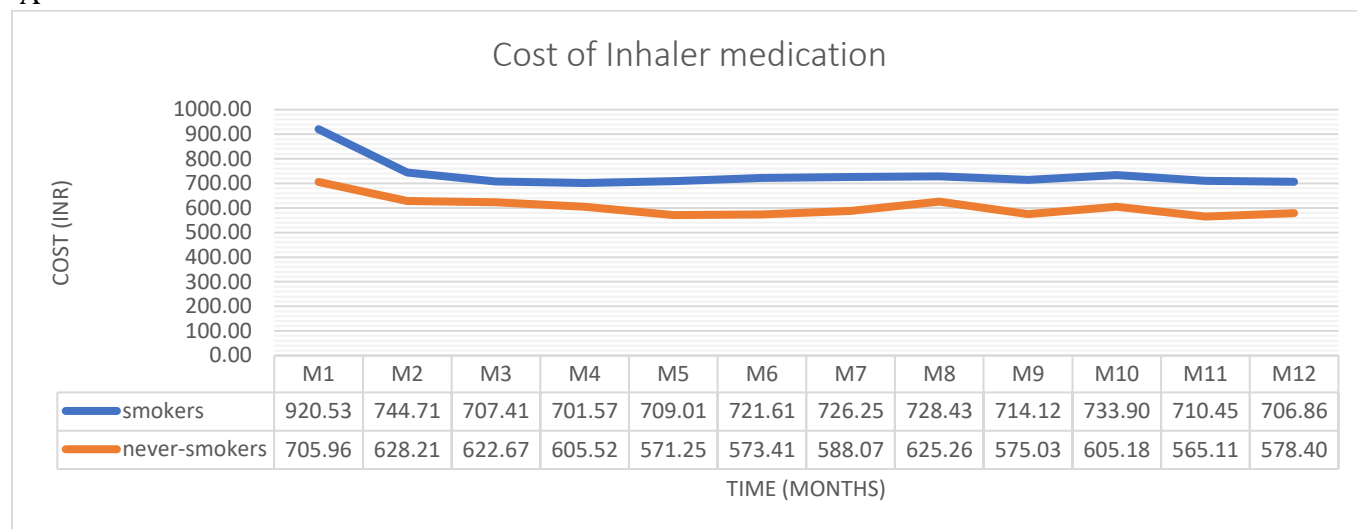


Figure 4. Comparison of Medication Cost in Smoker and Non-smoker COPD patient:

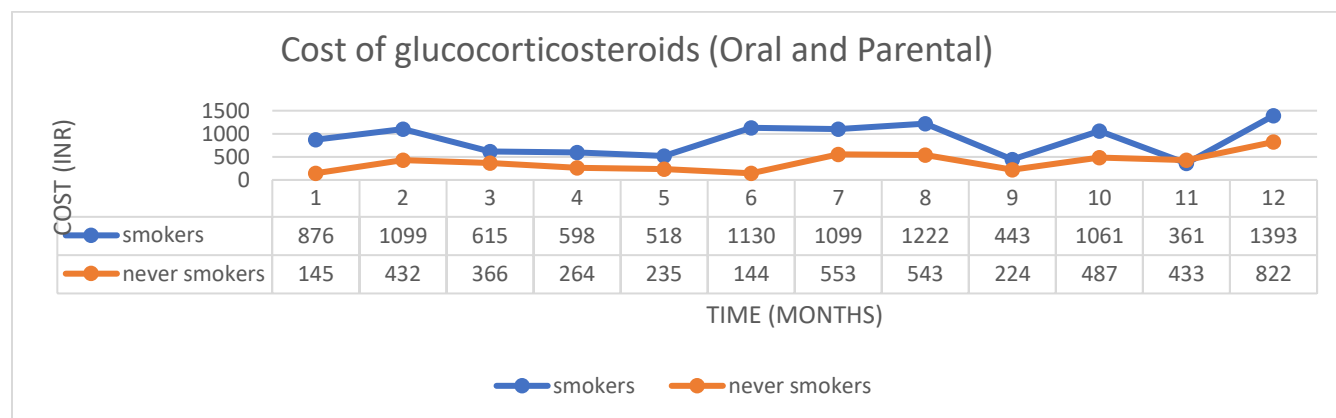
A) Cost of Inhaler medication in smoker cohort and never-smoker cohort, B) Cost of glucocorticosteroids (Oral and Parental) in

smoker cohort and never-smoker cohort, C) Cost of Antibiotics (Oral and Parental) in smoker cohort and never-smoker cohort

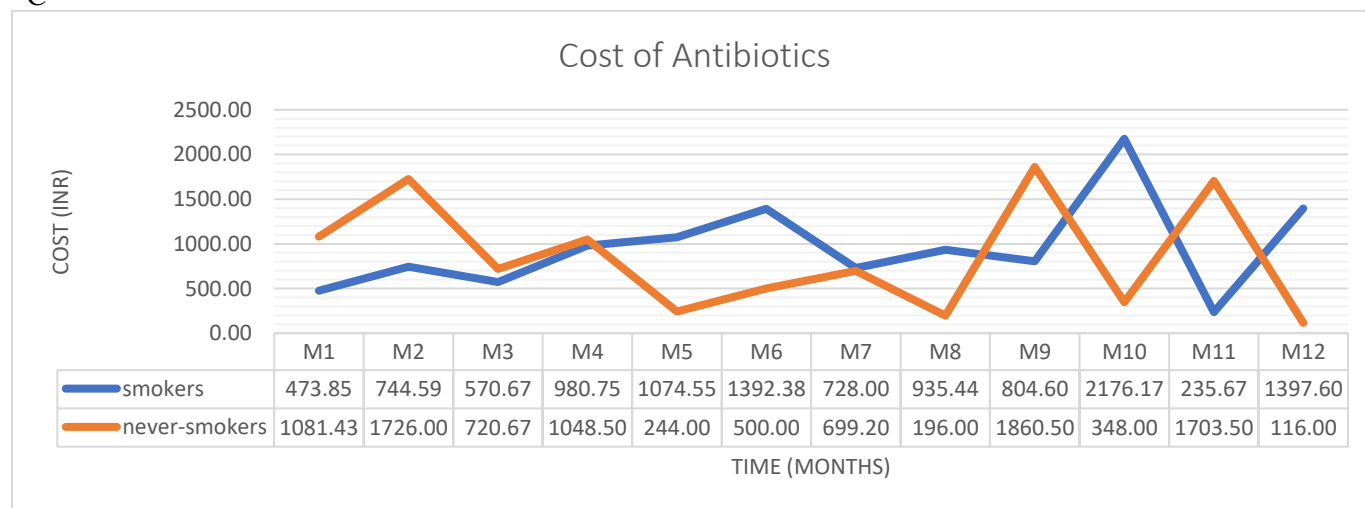
A



B



C



DISCUSSION

Cigarette smoking was a well-established risk factor for COPD, however recent literature shows multiple other etiological factors COPD can contribute or co-exist in a large group of COPD patients. The medication cost analysis from our study offers a perspective to the healthcare professionals and the patients on how smoking status influences the treatment cost on an annual basis. Although there was no clear consensus on treating non-smoking COPD patients differently, these patients were expected to show pathophysiological, histological, radiological, and biochemical differences. [24], [25], [26], [27], [28] This is the first study to quantify the medication cost in COPD patients based on smoking etiology.

Treatment cost in the management of COPD is relative to the severity of the disease. The frequency of exacerbations and hospitalizations drives the total cost of medication as the need for the parental route of medications increases. Patients with COPD were 2.3 times more likely to be admitted to the hospital at least once during the year, and those admitted had longer average lengths of stay.²⁹ Large-scale observational studies show the trend of cost increasing with COPD severity.^{30, 31} As high as 40.8% patients in this study were of severe and very severe category and 24.1% of them had at least 1 hospitalization in a year which is concurrent with previously published literature.

Similarly, a cost analysis study conducted in south India witnessed a steep increase in single hospitalization cost: (Stage II COPD - Rs. 3179.62 \pm 99.01, stage III -Rs.16414.79 \pm 8365.79 and stage IV - Rs.44077.16 \pm 15686.21.³² In this study, we observed that the moderate to severe category of COPD patients had to spend INR 7844 as the mean annual cost of medication but a very severe category of COPD patients had to spend INR 11323 for the same, which reiterates the fact that the cost burden increases with severity. The proportion of cost towards procuring inhaler medications was noted to be higher relative to the total cost spent on medications in both groups. However, the mean monthly inhaler medication cost differed significantly between the two groups (Non-smoker COPD patients = INR 603.67

\pm 154.36664, Smoker COPD patients = INR 785.40 \pm 288.74177, $p < 0.005$), during the study period. At the same time, there was no difference in the mean number and type of inhalers used in both groups.

Erdal *et al.*, in a study, explained the association between treatment cost and moderate to severe exacerbations in COPD patients. They reported that 6% of the annual treatment cost is attributed to acute exacerbations in stage 2 COPD patients and 13% in combined stage 3-4 COPD.³³ In this longitudinal, observational study, the patients reporting frequent hospitalizations and exacerbations had to incur incremental costs on both glucocorticosteroids and antibiotics. We noted the mean average number of hospitalizations and exacerbations among smoker COPD patients was 0.27 and 1.32 and it was 0.17 and 0.57 in the non-smoker cohort which was found to be statistically significant ($p < 0.05$).

In our study, the difference in mean total medication expenditure was majorly driven by relatively higher use of antibiotics, glucocorticosteroids (Oral and Parental) between the two cohorts. The use of oral and parental antibiotics and glucocorticosteroids was 21.40% in smoker COPD patients against 7.55% in non-smoker COPD patients of the total medication cost. ($p < 0.05$) The average cost incurred by COPD patients for parental glucocorticosteroids and antibiotics course during a single hospitalization was INR 14432 \pm 3877.13 and this remains to be similar for both groups (INR 13849 \pm 2732.31 in non-smokers and INR 14922 \pm 3122.34 in smokers). However, the annual cost spends on hospitalizations by non-smoking COPD patients was significantly lower than those of COPD patients with presence of smoking history. (INR \pm 6553.171.74 \pm 4108.52 in non-smokers and INR 9121.32 \pm 5213.72 in smokers, $p < 0.05$). This difference in both exacerbation and hospitalization frequency, during the study period, was significantly higher in the smoker COPD cohort than the non-smoker cohort which led to the incremental cost of medication.

There were a few limitations with this study. This was a single-center study and the findings cannot be extrapolated for all the centers as the prescription pattern, demographics of the patients, differ significantly from one hospital to another. However, a limited difference in the M.R.P (Maximum retail price) of the medications and use of similar agents for the management across the centers may prove our findings valid. The study tried to capture the cost of critical pharmacological agents (Inhalers, Antibiotics, IV, and Oral glucocorticosteroids) used to treat COPD but not the other components of the treatment cost which included traveling, loss of pay, and treatment burden co-morbidities. However, we believe these critical pharmacological agents were the cost drivers and that could well correlate to the overall cost burden. The study was carried out only for a short period of 12 months and we believe a long-term study with a larger group of a diverse population can be carried out to determine the precise differences in the medication cost but requires a longer duration and more number of follow-ups.

The mean monthly inhaler medication cost differed significantly between the two groups (Non-smoker COPD patients = INR 603.67±154.36664, Smoker COPD patients = INR 785.40± 288.74177, $p<0.005$), during the study period. At the same time, there was no difference in the mean number and type of inhalers used in both groups.

This difference in both exacerbation and hospitalization frequency was significantly higher in the smoker cohort than the non-smoker cohort which led to the incremental cost of medication. The use of oral and parental antibiotics and glucocorticosteroids was 21.40% in smoker COPD patients against 7.55% in non-smoker COPD patients of the total medication cost. ($p<0.05$) The average cost incurred by COPD patients for parental glucocorticosteroids and antibiotics course during a single hospitalization was INR 14432 ± 3877.13 and this remains to be similar for both groups (INR 13849 ± 2732.31 in non-smokers and INR 14922 ± 3122.34 in smokers).

The total mean medication expenditure for the entire twelve months in the non-smoker COPD

cohort was INR 9089.74 ± 4502.352 and it was INR 12234.82± 6553.171 in the smoker COPD cohort which is mentioned in Figure 3. The difference between these two groups was statistically significant. $p=0.001$).

On assessing the frequency of exacerbation, 13.8% of the non-smoker COPD group and 24.1% of the smoker COPD group were hospitalized at least once during the study period as mentioned in Table 2.

The mean monthly expenditure of inhaler medications, antibiotics, and glucocorticosteroids (oral and parental) was mentioned in Figure 4 (A-C).

The patients reporting frequent hospitalizations and exacerbations had to incur incremental cost on both glucocorticosteroids and antibiotics. This was due to the reason that the need for oral and parental antibiotics and glucocorticosteroids mounts higher during this period. The mean average number of hospitalizations and exacerbations among smoker COPD patients was 0.27 and 1.32 and it was 0.17 and 0.57 in the non-smoker cohort which was found to be statistically significant ($p<0.05$).

CONCLUSION

Healthcare expenditure to manage COPD was high and the number is expected to double. Hospitalizations and medication use accounted for most of these projected costs. Cost-minimization strategies are the need of the hour which must consider multiple factors including the disease burden, disease awareness, and the cost-effectiveness of available interventions. Smoking cessation programs proved to reduce costs related to COPD management and improved quality of life. It is important to hold consistent counseling programs to facilitate the understanding of how smoking status influences treatment outcomes. In brief, the present study verified that smoker COPD patients had to spend significantly higher on medications than non-smoker COPD patients. Because over 77% of the health care spending is with private hospitals and limited insurance penetration (<10%), a conscious effort to study and identify different phenotypes and their

treatment needs will ensure optimal use of medications. A comprehensive approach to minimize the frequency of hospitalizations and exacerbations will contain the medication cost as they were found to be the major driver of the treatment cost.

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