ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: https://ijrps.com

Comparison of Prevalence and Risk Factors in COPD Patients With and Without History of Smoking

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Article History:

Received on: 06 Jun 2020
Revised on: 17 Jul 2020
Accepted on: 21 Aug 2020

Keywords:

Chronic obstructive pulmonary disease, never smokers, prevalence, risk factors

ABSTRACT

A prospective cross-sectional study to compare the prevalence and risk factors in chronic pulmonary obstructive disease (COPD) patient with and without a history of smoking. This was an observational study conducted in the department of respiratory medicine, Chettinad Hospital and Research Institute (CHRI), Kancheepuram. A total of 206 patients with COPD, diagnosed as per GOLD criteria were enrolled in the study. Out of 206 COPD patients, 164 (79.61%) were men, and 42 (20.4%) were women and their mean age was 62.88 (± 9.53). The prevalence of COPD patients in smokers/ex-smokers were 125 (60.7%) and 81 (39.3%) in never smokers. There were 75 patients (92.59%) in the never smoker cohort and 72 patients (57.6%) in the ex-smoker/smoker cohort found to have at least one non-smoking risk factor for COPD. Biomass Exposure (39.50%), Passive Smoking (22.22%, P=), Co-existing Asthma (22.22%) were the non-smoking risk factors which were found to be present significantly higher in never smokers than smokers/ex-smokers, and the difference was statistically significant (<0.05). A higher proportion of severe patients were in smokers/ex-smokers than non- smokers (41.6% vs 27. 1%). Patients with moderate disease in both groups were found to be of equal proportion (12% vs 11. 11%). The results of the study reiterate that a significant proportion of COPD patients were never smokers and prevalence of non-smoking risk factors were more common in that population.

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ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v11i4.4625

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INTRODUCTION

COPD is a multifactorial disease affecting their quality of life by compromising the functional capacity of lungs. The pulmonary function loss is not entirely reversible, which is an essential characterization of the disease. The progressive and persistent air flow limitation is associated with the inflammatory response in the airways to noxious particles or gases (Singh *et al.*, 2019). It is prevalent for patients with COPD to have co-morbid conditions, and the quality of life of COPD patients would differ according to the severity of the disease. A 9-month observational study in India observed that the HRQOL (health-related quality of life) progressively worsened with increasing severity of the dis-

ease (Varughese and Jayakumari, 2017). The presence of co-morbid conditions can influence the hospitalization frequency, quality of life, disease progression, severity and frequency of exacerbations and cost of therapy.

Cigarette smoking has been established to be a prominent risk factor for COPD. Still, other factors such as air pollutants (indoor and outdoor) might also increase the risk of developing COPD. Smoking cessation is essential to improve the quality of life of the patients and provide synergy with the pharmacotherapy. It is now becoming evident that COPD could develop among non-smokers. This is substantiated with the results of the few epidemiological studies conducted in the past few years, where it observed a large proportion of COPD patients without a history of smoking (Lundback *et al.*, 2003; Lamprecht *et al.*, 2008; Celli *et al.*, 2005).

With the growing industrialization, nearly half the global population is exposed to smoke and biomass fuel compared to who smoke tobacco. This is reflecting on the increasing incidence of COPD in the non-smoking population, and it's mainly valid for rural women in developing countries. In the Rotterdam study of 14,619 participants, the proportion of female COPD participants without a history of smoking was 27.2 %, while this proportion was 7.3 % in males (Terzikhan *et al.*, 2016). Few of the reported risk factors in non-smokers developing COPD were genetics, outdoor air pollution, environmental smoke exposure (ETS), biomass fuel, occupational exposure, frequent respiratory infections in the early childhood and pulmonary tuberculosis (PTB). Passive smoking exposure also associated with the risk of developing COPD in non- smokers. Participants in the clinical trials were generally smokers, and very little is understood about the COPD patients with no history of smoking. The current observational study was conducted to evaluate the disease severity, proportion and risk factors of never smokers among COPD patients.

MATERIALS AND METHODS

This study was conducted in the department of respiratory medicine, Chettinad Hospital. The COPD patients who attend the OPD at the department of respiratory medicine between August 2019 to July 2020 were enrolled in the study after obtaining the informed consent. All patients with a confirmed diagnosis of COPD by clinical and spirometry GOLD guideline), of both genders were included in the study. The study has been reviewed and approved by the institutional ethics committee (525/IHEC/3-19). All study participants were subjected to a questionnaire for collecting demographics, details on exposure to various risk factors for COPD, number of hospitalizations, exacerbations, antibiotic use and Oral corticosteroids (OCS) in the previous one year (Trailing 12 months).

The data was entered in the Microsoft Excel, and the same was analyzed using statistical package for social sciences (SPSS) version 18. Chi-square test was used for testing association between categorical variables, and paired t-test was used to testing a significant difference between paired continuous variables. P-value < 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

In this study, a total of 206 COPD patients were enrolled with a mean age of 62.88 ± 9.53. In this cohort, there were 164 (79.61%) male and 42 (20.4%) female COPD patients. A significant proportion (43.20%) of patients were in the age group between 60 to 70 years. Mean duration of COPD (years since diagnosis of COPD) were 8.6±3.4 in the overall study population. Concerning severity of COPD, 18 (8.73%), 91 (44.17%), 74 (35.9%) and 23 (11.2%) were found to have moderate, severe and very severe COPD among the participants Table 1.

Table 1: Patient Characteristics

Characteristics	Mean, Patient Proportion
Age (Mean ± SD)	62.88 ± 9.53
<50 Years	25 (12. 13%)
≥50 - <60 Years	42 (20.38%)
≥60 - <70 Years	89 (43.20%)
≥70 - <80 Years	40 (19. 41%)
>80 Years	10 (4.85%)
Gender	
Male	164 (79.61%)
Female	42 (20.4%)
COPD Severity	
Mild	18 (8.73%)
Moderate	91 (44.17%)
Severe	74 (35.9%)
Very Severe	23 (11.2%)
Mean duration of COPD - Patients (Years)	8.6±3.4

Out of a total of 206 study participants, 125 (60.7%) were either ex-smokers or smokers, and 81 (39.3%) were non- smokers. A similar hospital-based study conducted in India reported a total of 47.6% of them were non- smokers (Ehrlich *et al.*, 2004). For many

social, cultural and environmental reasons, intensity and the prevalence of non-smoking risk factors of COPD differ widely between the regions, and so the varies incidences of COPD patients among never smokers. This was supported by few observational studies in which a relatively large proportion of COPD patients were non- smokers, ranging from 56.5% (Brashier *et al.*, 2007) to 68.6% (Mahmood *et al.*, 2017). Among ex-smokers/smokers, smoking prevalence in males were 99.2% (124/125) which was significantly higher than female COPD patients ($X^{2=}$75.150, P<0.005). Similarly, there was an equal number of non- smokers in both the genders (49.38% Male, 50.61% Female) (Table 2).

There were 75 patients (92.59%) in the never smoker cohort and 72 patients (57.6%) in the ex-smoker/smoker cohort found to have at least one non-smoking risk factor for COPD. The mean number of risk factor contributing to the development of COPD was found to be high in never smokers than ex-smokers/smokers (1.58 vs 0.8, p<0.05). The proportion of patients found to have 0, 1, 2 and 3 risk factors is illustrated in Figure 1. The difference was profound in patients carrying a total of 0, 2 and 3 risk factors between the two groups.

In this study, though the total steroid use between the groups was statistically significant, there were notable differences seen in patient proportion taking 3 and 4 courses of oral corticosteroids (OCS). 20.8% (n=3) & 7.2% (n=4) of ex-smokers/smokers and 4.93% (n=3) & 4.93% (n=4) of non- smokers had short courses of OCS in the last 12 months.

Distribution of COPD Patients Based on Disease Severity in Ex-smokers/Smokers and Non-Smokers

Out of the total of 206 COPD patients, a significant proportion of patients (>80%) were observed to be in both moderate and severe category. This pattern of disease severity was similar in the breakup analysis of ex-smoker/smoker and never smoker groups.

It was notable that severe COPD patients were 34.85% (41.6 vs 27.1) more in the ex-smoker/smoker group than the never smoker group. Nearly half of the patients in the non-smoker group fell in the moderate category, and the same was only 37.6% in the ex-smoker/smoker group which is (Figure 2).

A similar trend observed in the study conducted with 390 COPD patients, 56.94% of the non- smokers were categorized as moderate and 43.5% of smoker patients as severe (Kant *et al.*, 2019). There were an equal proportion of Mild and Very Severe COPD patients in both groups.

Prevalence of Non-smoking risk factors in Never Smokers

The non-smoking risk factors were reported to be relatively higher in never smokers. With regards to specific risk factors co-existing asthma, biomass exposure and exposure to indoor smoke (Passive smoking) were found to be present significantly higher in non- smokers (Table 3). Other non-smoking risk factors for COPD were noted to be numerically more significant with non- smokers; however, it was found to be statistically not significant. Occupational exposure and outdoor population were the common non-smoking risk factor among both the groups.

There were only a few epidemiological studies published in India and the results of those varied to a large extent. The variation of prevalence reported in India is because of varying socio demographic profiles, cultural practices and ethnicities. Also, the prevalence of COPD estimates was not accurate. There were few large-scale epidemiological studies conducted in India witnessed the prevalence varied significantly (Mahesh *et al.*, 2009; Jindal *et al.*, 2006). In one of the epidemiological studies conducted in India, in 2012, the prevalence of COPD was found to be ranging from 1.1% in Mumbai to 10% in Trivandrum (Jindal *et al.*, 2012). In a similar global study conducted by Burney et al., the prevalence of COPD in Indian cities was found to be 6.25% (Pune), 6.8 % (Mumbai), and 16.05% (Srinagar) (Burney *et al.*, 2014). They also established a strong association with poverty and smoking. This is more relevant to India as we have a large group of people living under below poverty line, and it is also important how this is mediated.

During their lifetime, women are exposed to biomass smoke for 30 to 40 years, which is equivalent to 60,000 h of exposure or inhaling a total volume of 25 million L of polluted indoor air (Salvi and Barnes, 2010) (Mohan *et al.*, 2016). Reported an interesting outcome that protease-antiprotease balance in COPD was in tobacco exposure and biomass exposure but was different than the controls (Mohan *et al.*, 2016). The high incidence of COPD in non-smokers was associated with indoor air pollution lead by biomass combustion (Bakr and Elmahallawy, 2012). In one of the studies conducted in India, 53.98% of the study population was found to be exposed to biomass (Gordon *et al.*, 2014). Though the proportion of patients with a history of biomass exposure was relatively lesser than reported earlier, 39.5% of the non- smokers carry it as one of the risk factors.

The burden of non-smoking COPD in developing

Table 2: Proportion of COPD patients according to age, smoking and smoking status.

		Ex-smokers/Smokers	Never Smokers
Number of Patients (n=206), %		125 (60.7%)	81 (39.3%)
Age ± Mean		62.54 ±9.738	63.42 ±9.381
Sex, %	Male	124 (99.2%)	40 (49.38%)
	Female	1 (0.8%)	41 (50.61%)

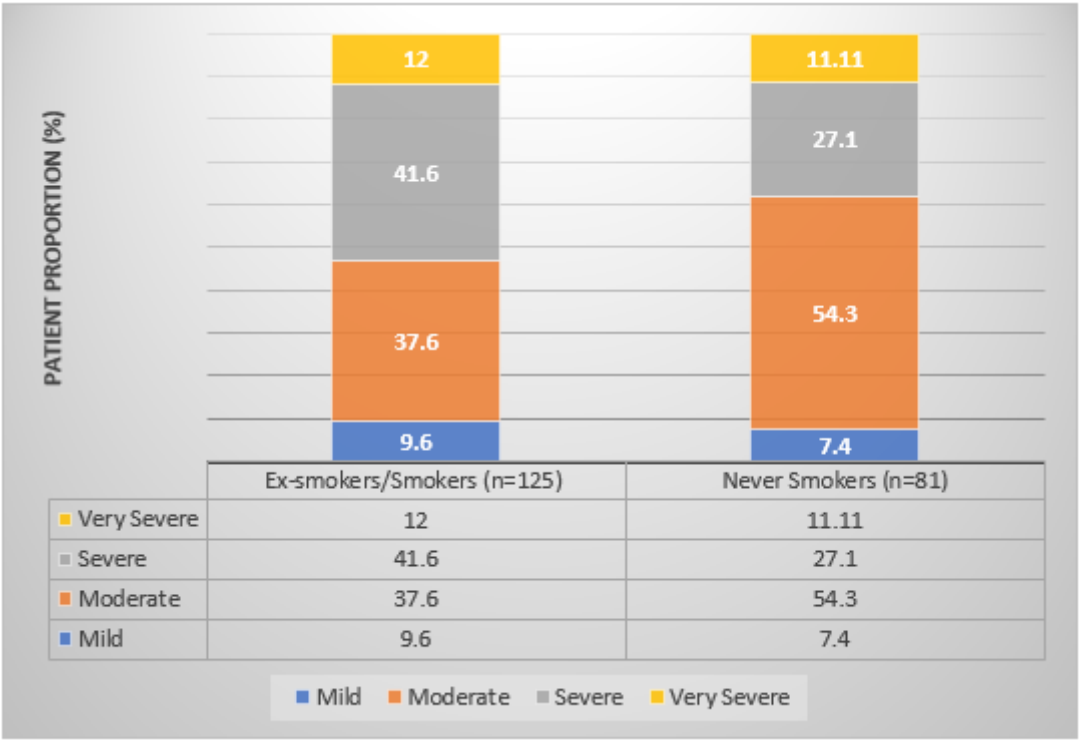

Figure 1: Distribution of Ex-smokers/Smokers and Never Smokers according to number of non-smoking risk factors for COPD

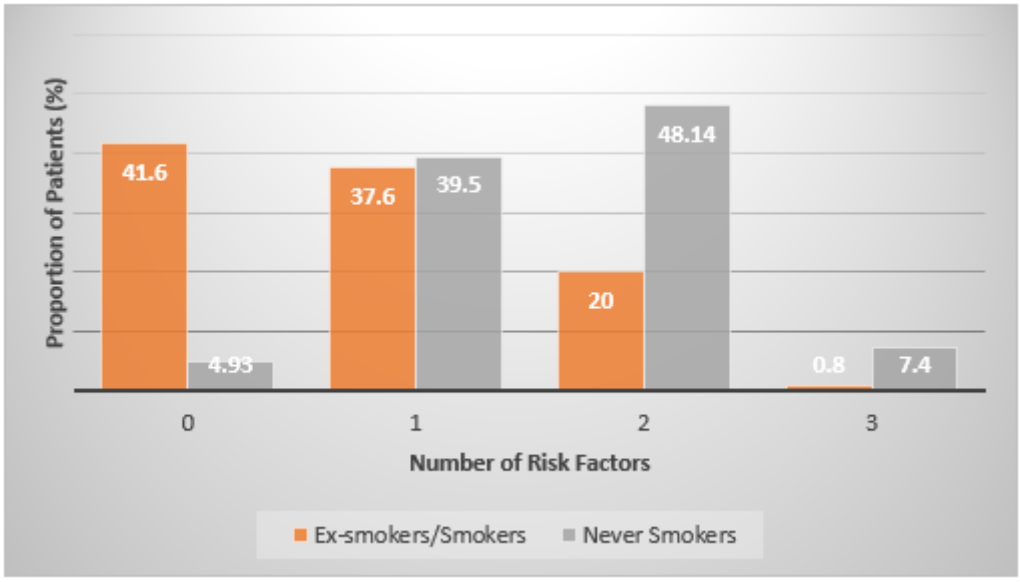

Figure 2: Mean Number of Non-smoking risk factors in both Ex-smokers/smokers and Never Smokers:

Table 3: Prevalence of Non-smoking risk factors in Ex-smokers/Smokers and Never Smokers:

S.No	Non-smoking Risk Factors	Total study population (n=206	(%)	Ex-smokers /Smokers (n=125)	(%)	Never Smokers (n=81)	(%)	P	X2
1	Outdoor pollution	44	21.35	23	18.4	21	25.92	0. 198	1.657
2	Pre-treated TB	29	14.07	19	15. 2	10	12.34	0.565	0.331
3	Co-existing Asthma	25	12.13	7	5.6	18	22.22	0.000	12.736
4	Biomass Exposure	39	18.93	7	5.6	32	39.50	0.000	36.816
5	Exposure to indoor smoke (Passive Smoking)	23	11.16	5	4	18	22.22	0.000	16.455
6	Frequent lower respiratory tract infection during childhood	4	1.94	3	2.4	1	1.23	0.554	0.351
7	Occupational Exposure	56	27.18	32	25.6	24	29.62	0. 525	0.403

nations was very high. In a study conducted in India (Mahmood *et al.*, 2017), it was found that only 9.73% of the non-smokers were found to have occupational exposure at the baseline. Still, a study in 300 Egyptian patients reported a large population (41.7%) caring occupational exposure as one of the risk factors in never smokers (Bakr and Elmahallawy, 2012). The present observational study reported a sizable proportion of COPD patients with occupational exposure. However, there was no difference between the ex-smoker/smoker group and non- smokers (27.1 vs 29.6 p = 0.403).

Outdoor air pollution is another significant contributor in the developing countries owing to rapid industrialization and increasing use of automobiles. The connection between elevated concentrations of outdoor air pollution and COPD exacerbation and worsening COPD disease status is proved to be accurate, already (Arbex *et al.*, 2009). The reported prevalence of outdoor air pollution in India was highly variable between 3.54% (Mahmood *et al.*, 2017) and 19.8% (Shameem *et al.*, 2015). A meta-analysis, published in 2014, reported the association of outdoor air pollution with a rising trend of COPD incidence and prevalence (Song *et al.*, 2014).

History of pulmonary tuberculosis (PTB) is the most common co-morbid condition found to be present in non- smoking COPD patients. The impairment of respiratory function in pulmonary TB patients is reported very long ago—the airflow obstruction in 61% of 1533 TB patients. Lam et al. reported that a history of TB was an independent predictor of airflow limitation with OR 1.37 after adjusting sex, age and smoking exposures (Lam *et al.*, 2010). PTB was present in 32.74% and 21.9% of never smoker COPD patients in Indian Studies (Mahmood *et al.*, 2017; Shameem *et al.*, 2015). In this study, we report the prevalence of PTB as a risk factor in non- smokers and ex-smokers/smokers to be similar (12.34% vs 15. 2% p=0.331). Though it is the lowest proportion reported, the total number of PTB patients were nearly the same as reported by (Kant *et al.*, 2019). This becomes more important in a country like India, where the disease is endemic (Mahmood *et al.*, 2017).

Asthma and COPD were chronic respiratory diseases affecting larger and smaller airways, and the clinical manifestations overlap with each other. Long-standing asthma as a risk factor for COPD. The proportion of patients with asthma develop COPD was reported to higher. In observational studies conducted in India, it was found that asthma was the risk factor for about 14.16% (P=0.003) and 37.50%(P<0.0001) of non-smoking patients to develop COPD (Mahmood *et al.*, 2017; Shameem

et al., 2015). In our study, we witnessed 39.5% of non-smokers had co-existing asthma as a risk factor which was statistically more significant than smokers (P<0.00) X^2=12.736. An epidemiological study reported that having asthma increases the risk up to twelve-fold for developing COPD over time than those without asthma, after adjusting for smoking (Silva *et al.*, 2004). Frequent lower respiratory tract infection during childhood were least commonly reported risk factor in both groups (3 in smokers/smokers vs 1 in never smokers).

CONCLUSION

Chronic Obstructive Pulmonary Disease is a multifactorial disease affecting the quality of life by compromising the functional capacity of lungs. The most common and established risk factor for COPD is cigarette smoking, but also other factors such as indoor and outdoor air pollutants might increase the risk of COPD. The prevalence of non-smoking COPD in developing countries was very high, and there was found to be widely variable between studies. Biomass fuel is the primary source for cooking in developing countries. COPD caused by exposure to smoke from biomass fuels were mostly seen in women with the presence of lower BMI and more clinical symptoms, and the co-morbidities were mostly allergic rhinitis. Bronchial asthma and the COPD classification were mostly Grades B, and D. COPD is no more solely confirmed or diagnosed with FEV1. Assessment of symptoms and exacerbations were vital to diagnose and determine the severity of the COPD of a patient. The studies have begun to study the phenotypic differences recently. There were different phenotypes proposed in the last few years, but the evidence support to classify the patient group was inconclusive. The process of phenotyping emerges as a need to stratify patients with a similar presentation to provide them with optimum care. Co-morbidities should be actively sought and duly addressed therapeutically. Differential therapy response cannot be ruled out in COPD patients of with and without a smoking history. Further research in non-smoking COPD population would facilitate in developing an appropriate treatment region for these two groups of COPD patients.

ACKNOWLEDGEMENT

We wish to thank the Faculty of Pharmacy, Vels Institute of Science, Technology and Advanced Sciences (VISTAS), for research facilities. Besides, appreciation is expressed to participants, respiratory therapists and respiratory medicine postgraduate students who assisted in the study.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of interest

The authors declare that they have no conflict of interest for this study.

REFERENCES

Arbex, M. A., de Souza Conceicao, G. M., Cendon, S. P., Arbex, F. F., Lopes, A. C., Moyses, E. P., Santiago, S. L., Saldiva, P. H. N., Pereira, L. A. A., Braga, A. L. F. 2009. Urban air pollution and chronic obstructive pulmonary disease-related emergency department visits. *Journal of Epidemiology & Community Health*, 63(10):777–783.

Bakr, R. M., Elmahallawy, I. I. 2012. Prevalence characteristics of COPD in never smokers. *Egyptian Journal of Chest Diseases and Tuberculosis*, 61(3):59–65.

Brashier, B., Gangavane, S., Valsa, S., Gaikwad, S. N., Ghorpade, S. V., Mandrekar, S. 2007. Almost half of the patients treated for pulmonary tuberculosis (TB) show evidence of obstructive airways disease (OAD). pages 15–19, Stockholm, Sweden. European Respiratory Society Annual Congress.

Burney, P., Kato, B., Janson, C., Mannino, D., Studnicka, M., Tan, W., Bateman, E., Koçabas, A., Vollmer, W. M., Gislason, T., Marks, G., Koul, P. A., Gnatiuc, L., Buist, S. 2014. Chronic obstructive pulmonary disease mortality and prevalence: the associations with smoking and poverty: a BOLD analysis—authors' reply. *Thorax*, 69(9):869–870.

Celli, B. R., Halbert, R. J., Nordyke, R. J., Schau, B. 2005. Airway obstruction in never smokers: Results from the Third National Health and Nutrition Examination Survey. *The American Journal of Medicine*, 118(12):1364–1372.

Ehrlich, R. I., White, N., Norman, R., Laubscher, R., Steyn, K., Lombard, C., Bradshaw, D. 2004. Predictors of chronic bronchitis in South African adults. *The International Journal of Tuberculosis and Lung Disease*, 8(3):369–376.

Gordon, S. B., Bruce, N. G., Grigg, J., Hibberd, P. L., Kurmi, O. P., Lam, K. B. H., Bar-Zeev, N. 2014. Respiratory risks from household air pollution in low and middle-income countries. *The Lancet Respiratory Medicine*, 2(10):823–860.

Jindal, S. K., Aggarwal, A. N., Chaudhry, K., Chhabra, S. K., Souza, G. A., Gupta, D., Vijayan, V. K. 2006.

Jindal, S. K., Aggarwal, A. N., Gupta, D., Agarwal, R., Kumar, R., Kaur, T., Chaudhry, K., Shah, B. 2012. Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis in adults (INSEARCH). *The International Journal of Tuberculosis and Lung Disease*, 16(9):1270–1277.

Kant, S., Bajpai, J., Bajaj, D., Pradhan, A., Srivastava, K., Pandey, A. 2019. Clinical, demographic and radiological profile of smoker COPD versus non-smoker COPD patients at a tertiary care center in North India. *Journal of Family Medicine and Primary Care*, 8(7):2364.

Lam, K. B. H., Jiang, C. Q., Jordan, R. E., Miller, M. R., Zhang, W. S., Cheng, K. K., Adab, P. 2010. Before TB, smoking, and airflow obstruction: a cross-sectional analysis of the Guangzhou Biobank Cohort Study. *Chest*, 137(3):593–600.

Lamprecht, B., Schirnhofer, L., Kaiser, B., Buist, S., Studnicka, M. 2008. Non-reversible airway obstruction in never smokers: Results from the Austrian BOLD study. *Respiratory Medicine*, 102(12):1833–1838.

Lundback, B., Lindberg, A., Lindstrom, M., Ronmark, E., Jonsson, A. C., Jonsson, E., Larsson, L. G., Andersson, S., Sandstrom, T., Larsson, K. 2003. Not 15 But 50% of smokers develop COPD?—Report from the Obstructive Lung Disease in Northern Sweden Studies. *Respiratory Medicine*, 97(2):115–122.

Mahesh, P. A., Jayaraj, B. S., Prahlad, S. T., Chaya, S. K., Prabhakar, A. K., Agarwal, A. N., Jindal, S. K. 2009. Validation of a structured questionnaire for COPD and prevalence of COPD in rural area of Mysore: A pilot study. *Lung India*, 26(3):63.

Mahmood, T., Singh, R., Kant, S., Shukla, A., Chandra, A., Srivastava, R. 2017. Prevalence and etiological profile of chronic obstructive pulmonary disease in nonsmokers. *Lung India*, 34(2):122.

Mohan, A., Sharma, M., Uniyal, A., Borah, R., Luthra, K., Pandey, R. M., Madan, K., Hadda, V., Guleria, R. 2016. Variability in proteinase-antiproteinase balance, nutritional status, and quality of life in stable chronic obstructive pulmonary disease due to tobacco and nontobacco etiology. *Lung India*, 33(6):605.

Salvi, S., Barnes, P. J. 2010. Is Exposure to Biomass Smoke the Biggest Risk Factor for COPD Globally? *Chest*, 138(1):3–6.

Shameem, M., Alam, M., Ahmad, Z., Ejazi, A. 2015. COPD in Non-smokers-Prevalence and Risk Factors. *British Journal of Medicine and Medical Research*, 8(2):165–176.

Silva, G. E., Sherrill, D. L., Guerra, S., Barbee, R. A. 2004. Asthma as a Risk Factor for COPD in a Longitudinal Study. *Chest*, 126(1):59–65.

Singh, D., Agusti, A., Anzueto, A., Barnes, P. J., Bourbeau, J., Celli, B. R., Criner, G. J., Frith, P., Halpin, D. M. G., Han, M., Varela, M. V. L., Martinez, F., de Oca, M. M., Papi, A., Pavord, I. D., Roche, N., Sin, D. D., Stockley, R., Vestbo, J., Wedzicha, J. A., Vogelmeier, C. 2019. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. *European Respiratory Journal*, 53(5):1900164.

Song, Q., Christiani, D., XiaorongWang, Ren, J. 2014. The Global Contribution of Outdoor Air Pollution to the Incidence, Prevalence, Mortality and Hospital Admission for Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. *International Journal of Environmental Research and Public Health*, 11(11):11822–11832.

Terzikhan, N., Verhamme, K. M. C., Hofman, A., Stricker, B. H., Brusselle, G. G., Lahousse, L. 2016. Prevalence and incidence of COPD in smokers and non-smokers: the Rotterdam Study. *European Journal of Epidemiology*, 31(8):785–792.

Varughese, J. D., Jayakumari, S. 2017. A Prospective observational study on health-related quality of life in chronic obstructive pulmonary disease patients based on severity. *Asian Journal of Pharmaceutical and Clinical Research*, 10(8):244.