OBJECTIVE: The most important risk factor for chronic obstructive pulmonary disease (COPD) is smoking. However, more than 25% of patients do not have a history of smoking. The intent of this study is to identify characteristics of COPD patients that are non-smokers.

MATERIAL AND METHODS: The records of patients with COPD were retrospectively reviewed. Smoking history, comorbidities, exacerbations, biomass, and environmental tobacco smoke (ETS) exposures were identified. Also, age, gender, pulmonary function test (PFT) values, modified Medical Research Council (mMRC) dyspnea scores were recorded. Non-smokers exposed to any of the COPD risk factors above were grouped and the data were analyzed to determine the specific characteristics of COPD that applied to them.

RESULTS: A total of 706 COPD patients were analyzed with a mean age of 67.2 ± 9.4. Of these patients, 93 (13.2%) were female and 613 (86.8%) were male. Of the 706 patients, 128 (18.1%) were non-smokers. The percentage of male patients having COPD was significantly lower in the non-smoker group ($P < .001$). However, biomass, ETS exposure in childhood, and a history of previous respiratory infection were significantly higher in the non-smoker group ($P < .001$). The mean body mass index (BMI) was greater in non-smokers than smokers.

CONCLUSION: Non-smokers with COPD have more biomass, ETS exposure, and infection history in childhood. They also have less impairment of airflow limitation, better symptom scores, and greater BMIs. Smoking history can be used to determine a different phenotype.

KEYWORDS: Chronic obstructive pulmonary disease, smoker, non-smoker

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the primary causes of morbidity and mortality worldwide, with many people dying at an early age due to COPD. The most important risk factor for COPD is smoking. The prevalence of COPD is directly related to the frequency of smoking. The major risk factor in developing COPD is cigarette smoking. However, more than 25% of patients do not have a history of smoking. COPD has been described in studies with different frequency in non-smokers. Data related to non-smokers are limited. COPD studies generally include smokers and/or ex-smokers. Other contributing factors to developing COPD, though to a lesser degree are: occupational exposure, past/childhood respiratory diseases, indoor and outdoor air pollution, passive smoke exposure, biomass exposure, age, female gender, low socio-economic status, malnutrition, inadequate lung development, genetic disorders, and asthma.

In developing countries, exposure to fuels used in cooking (caused by the burning of wood and other fuels) is an additional contributing factor for the development of COPD in women. In recent years, the term ‘phenotype’ has been used to describe different COPD subgroups. Like the pulmonary-cachexia phenotype of COPD-bronchiectasis overlap syndrome, non-smoker COPD patients have also been described as a separate phenotype in some publications. The intent of this study is to identify the general characteristics of non-smoking COPD patients and to determine any significant differences between non-smoking patients and those who smoke.

MATERIAL AND METHODS

The records of patients who were followed up and/or diagnosed with COPD from January to December 2018 in a tertiary research and training hospital outpatient clinic were retrospectively reviewed. To be included in the study, a patient required a ratio of forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) of 70% or less after bronchodilator use.
The authors excluded any patients from the study who had:

- An exacerbation within 4 weeks of admission, and
- Other lung diseases such as pulmonary tuberculosis, pneumosilicosis, interstitial lung disease, pleural effusion, or a history of pneumonectomy.

The following patient characteristics were identified for each subject included in the study: smoking history, comorbidities, any acute exacerbation of COPD (AeCOPD) during the last year, presence of bronchiectasis, biomass and passive tobacco smoke exposures, educational level, socio-economic status, age, gender, FEV1, FVC, FEV1/FVC ratio values, modified “Medical Research Council” (mMRC) scores, body mass index (BMI) value (kg/m²), any pulmonary infections prior to the age of 10 years, pulmonary symptoms (cough, sputum, and dyspnea), any physician diagnosis history of tuberculosis and comorbidity (heart disease, hypertension (HT), diabetes).

- Patients were classified into “smoker,” “ex-smoker,” and “non-smoker” categories based on the following definitions:
  - “Non-smoker”: someone who had smoked an average of less than 1 cigarette per day for less than 1 year or had never smoked,
  - “Ex-smokers”: those who had stopped smoking at least 12 months prior to the interview, and
  - “Smokers” (current or former smokers): persons who had smoked greater than 20 packs of cigarettes in a lifetime or greater than 1 cigarette per day for a year.

Non-smokers exposed to COPD risk factors were grouped and their data were analyzed to determine the specific characteristics of COPD in these subjects in comparison to smokers with COPD.

Exposure to environmental tobacco smoke (ETS) during childhood was considered positive if a household member smoked cigarettes in the home during the subject’s childhood.

**Pulmonary Function Tests (PFTs)**

PFTs had been performed using a ZAN 300 device (ZAN Messgerate, Oberthulba, Germany) in the sitting position. The highest value of FEV1 and FVC from at least 3 technically satisfactory maneuvers differing by less than 5% was the value used for the study for that particular patient.

**Assessment of Dyspnea**

“mMRC” dyspnea scale was used to determine the severity of patients’ shortness of breath. The scale consists of 5 items ranging between 0 and 4. The score “0” represents the best level, whereas the score “4” indicates the poorest.

**RESULTS**

A total of 706 COPD patients with a mean age of 67.2 ± 9.4, including 93 (13.2%) female and 613 (86.8%) males were included in the study retrospectively. Table 1 presents the general characteristics of the cases. 578 (81.9%) of all cases had a history of smoking. Of these 578 patients, 322 (45.7% of total subjects and 55.7% of smokers) were classified as “smokers” and 256 (36.2% of the total sample and 44.3% of the smokers) were classified as “ex-smokers.” Of the 706 patient sample, 128 (18.1%) had never smoked.

### Table 1. General Properties of all Cases

|                          | n  | %    |
|--------------------------|----|------|
| Gender                   |    |      |
| Male                     | 613| 86.8 |
| Female                   | 93 | 13.2 |
| Smoking history          |    |      |
| Smoker                   | 322| 45.6 |
| Ex-smoker                | 256| 36.3 |
| Non-smoker               | 128| 18.1 |
| History of tuberculosis  | 109| 15.4 |
| Biomass exposure         | 30 | 4.2  |
| Acute eCOPD in last year | 55 | 7.8  |
| Pulmonary infection at childhood | 16 | 2.3  |
| ETS in childhood caused by | 101 | 14.3 |
| Mother                   | 22 | 3.1  |
| Father                   | 79 | 11.2 |
| Comorbid diseases (n = 636) | 348 | 54.7 |
| HT                       | 202| 31.8 |
| DM                       | 93 | 14.6 |
| CHF                      | 71 | 11.2 |
| CAD                      | 65 | 10.2 |
| Lung cancer              | 32 | 5    |
| Bronchiectasis           | 8  | 1.3  |
| Pulmonary symptoms (n = 682) |     |      |
| Cough                    | 230| 33.7 |
| Sputum                   | 480| 70.4 |
| Dyspnea                  | 644| 94.4 |

The mean age was 67.2 ± 9.0 for “smokers” and 67.4 ± 11.3 for “non-smokers.” There was no statistically significant difference in age between the 2 groups. There was a significant difference in gender distribution and there were significantly more females in the “non-smoker” group than in the “smoker” group (P < .001). In addition, biomass exposure, ETS exposure in childhood, and history of previous respiratory infection were significantly higher in the “non-smoker” group (all P < .001). The mean BMI was higher in the “non-smoker” (27.0 ± 6.5) group than in the “smoker” (24.5 ± 5.8) (P < .001) (Table 2).

In the “non-smoker” group, the percentage of patients who exhibited more severe symptoms (mMRC 3-4) was significantly lower than in the “smoker” group. The sputum symptom was significantly lower in the “non-smoker” group. The respiratory function parameters of FEV1 percentage (FEV1%) and FEV1/FVC ratio were compared between the 2 groups and found to be significantly greater in the non-smokers vs. smokers (Table 3).

Similarly, both the non-smoker and smoker groups had a lower level of education (primary school, literate or illiterate) (92.1%). Although it was not statistically significant, the number of high school and/or university graduates was higher.
for the non-smokers. The income levels for patients in both groups were similar.

**DISCUSSION**

In the study, 80-90% of all COPD cases are attributed to smoking and there is a positive relationship between smoking and COPD prevalence.13 COPD can also be seen in non-smokers. Although there are studies about the role of risk factors in non-smoker COPD patients, we also aimed to determine the different characteristics and risk factors for non-smoker COPD patients.

When compared the smoker group with the non-smoker group, biomass exposure, childhood ETS exposure from parents, history of previous respiratory infection, and the presence of bronchiectasis were higher. The rate of female patients was higher. In addition, the rate of patients who were more symptomatic was lower and FEV1% and FEV1/FVC ratios were higher. BMI was also higher in the non-smoker group.

While the major risk factor for COPD is smoking, 25-45% of patients with COPD have never smoked,6,9 more than 82% of our cases have a history of smoking and 18% are a non-smoker.

The rate of non-smokers in patients with COPD has been given at varying rates in various studies (9.4-68.6%). Especially in studies performed in India, it is stated that such higher rates were seen due to the fact that some studies in India were performed with respiratory system questionnaires. The rate decreases in studies where the diagnosis is made by spirometry.14,15 A lower rate was found in our study as in the west.

In our study, a history of tuberculosis was detected in 21.1% of non-smoker cases and was found to be significantly higher

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**Table 2. General Properties of the Cases**

|                        | Non-smoker (n = 128) | Smoker/ex-smoker (n = 578) | P     |
|------------------------|----------------------|-----------------------------|-------|
| Gender                 |                      |                             |       |
| Female                 | 53 (41.4)            | 40(6.9)                     | .000  |
| Male                   | 75(58.6)             | 538(93.1)                   |       |
| History of tuberculosis| 27(21.1)             | 82(14.2)                    | .069  |
| Biomass exposure       | 25(19.5)             | 5(0.9)                      | .000  |
| Pulmonary infection at childhood | 14(10.9) | 2(0.3)                      | .000  |
| ETS in childhood caused by |                    |                             |       |
| Mother                 | 15(11.7)             | 7(1.2)                      | .000  |
| Father                 | 50 (39.1)            | 29 (5.0)                    | .000  |
| Comorbid diseases*     | 75(66.4)             | 273(52.2)                   | .006  |
| HT                     | 43(38.1)             | 159(30.4)                   | >.05  |
| DM                     | 22(19.5)             | 71(13.6)                    | >.05  |
| CHF                    | 20 (17.7)            | 51(9.8)                     | .023  |
| CAD                    | 11 (9.7)             | 54(10.3)                    | >.05  |
| Bronchiectasis         | 6 (5.3)              | 2(0.4)                      | .001  |
| Lung cancer            | 2 (1.8)              | 30(5.7)                     | >.05  |
| Pulmonary symptoms     |                      |                             |       |
| Cough                  | 60(48.4)             | 170(30.5)                   | .000  |
| Sputum                 | 75(60.5)             | 405(72.6)                   | .008  |
| Dyspnea                | 116(93.5)            | 528(94.6)                   | >.05  |
| Acute eCOPD in last year mean | 15(11.7) | 40(6.9)                     | .099  |
| mMRC                   |                      |                             |       |
| 0-2                    | 29(23.0)             | 84(14.8)                    |       |
| 3-4                    | 97(77.0)             | 484(85.2)                   | .033  |
| Body mass index        | 27.0 ± 6.5           | 24.5 ± 5.8                  | .000  |

Numbers with significant p values are shown in bold.

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**Table 3. PFT of all Cases**

|                          | Non-smoker | Smoker/Ex-smoker | P     |
|--------------------------|------------|------------------|-------|
| FEV1 (%)                 | 39.1 ± 16.0| 34.0 ± 14.4      | .000  |
| FEV1 (L)                 | 0.89 ± 0.41| 0.91 ± 0.41      | .688  |
| FVC (%)                  | 51.0 ± 17.0| 48.2 ± 17.0      | .091  |
| FVC (L)                  | 1.53 ± 0.66| 1.66 ± 0.65      | .045  |
| FEV1/FVC                 | 59.7 ± 12.0| 54.3 ± 10.3      | .000  |
than smoker cases. This rate is even higher in studies performed in India and Africa.\textsuperscript{14,16} This is attributed to the high prevalence of pulmonary tuberculosis in these countries. Although the prevalence of pulmonary tuberculosis has decreased in our country, its high rate can be attributed to the high prevalence of tuberculosis in the past.

Biomass exposure may be the greatest risk factor for COPD globally.\textsuperscript{17} Biomass exposure was present in 4.2\% of all COPD cases, while this rate was 19.5\% in the non-smoker group. In studies performed in India, this rate rises to 50\% because biomass is used for heating and cooking in 70\% of the people in India.\textsuperscript{14} However, in a study conducted in Finland and Sweden in 2001, a similar relationship was found, although the rate was not so high.\textsuperscript{18}

ETS exposure is known to be a risk factor for COPD.\textsuperscript{19} The prevalence of childhood ETS exposure in non-smokers was significantly higher (approximately 3 times) than the others in this study. In other studies, data on ETS are not included much. However, we found that ETS is also an important cause of COPD in non-smokers.

In this study, we detected a history of pulmonary infection in 10.9\% of patients with non-smoker COPD in childhood. And this rate was found statistically significantly higher when compared to the rate in smokers. In another study, we found that severe pulmonary infection in childhood is associated with decreased lung function.\textsuperscript{20}

Male gender, older age, occupational exposure, and low socio-economic status are some of the other known risk factors of COPD. More than 80\% of the patients included in our study were male. In the study of Jing et al., almost all cases of smoker COPD were male, while the rate of men in non-smokers was also reported to be much higher than in our study. Although non-smoker COPD cases were reported to be younger than smokers, the mean age of our cases was similar in both groups.\textsuperscript{11,21} In the study of Jing et al.,\textsuperscript{21} the mean age of smokers and non-smoker COPD was also similar.

Although lower socio-economic status was reported to be an important risk factor for COPD in non-smokers, income levels were similar in smokers and non-smokers in our study.

Similar to the previous studies, FEV/FVC and FEV1\% values were also higher in the non-smoker group in our study.\textsuperscript{15,22} In other words, airway restriction is less in non-smoker patients. This has been attributed to the chronic inflammation, narrowing of the small airways, destruction of the parenchyma, and reduction of the alveolobronchial handles caused by smoking in smokers.

In our study, it was observed that the non-smoker group had better symptom scores. The rate of patients with mMRC score 0-2 was higher in the non-smoker group, and the rate of patients with mMRC score 3-4 (more symptomatic) was lower in the non-smoker group. Whereas, in the study of Jing et al., no difference was observed between the non-smoker and smoker groups when the patients were divided based on mMRC scores lower and higher than 1.\textsuperscript{22}

Chronic cough and sputum due to increased mucus production in major airways are the main symptoms of COPD.\textsuperscript{23} When we evaluated all our cases, it was found that respiratory complaints (cough, sputum, dyspnea) were higher than the literature.\textsuperscript{22,24} In their study, Jing et al. reported a higher prevalence of both cough and sputum in smokers. In our study, we found that those sputum symptoms were higher in the smokers but cough symptoms were higher in the non-smoker.\textsuperscript{22} Bajpai et al. found that the cough symptom was higher in the non-smokers, and the complaints of shortness of breath and sputum were higher in the smokers.\textsuperscript{15} We conclude that the cough symptom may be less pronounced in smokers because it is attributed to smoking. In addition, cough symptoms may be higher in our non-smoker group because of the higher frequency of bronchiectasis.

Cheng et al. reported that patients with frequent AeCOPD history had more smoking history.\textsuperscript{24} However, in our study, no significant difference was observed between the non-smoker and smoker groups in the last 1 year.

It has long been found that nicotine has mild metabolic effects and suppresses appetite.\textsuperscript{25} In our cases, non-smokers were also fatter than those who smoked, and this result was found in the study of Ji et al. Our finding was similar to that study.\textsuperscript{21}

The most common additional diseases in COPD patients were: HT, diabetes mellitus (DM), congestive heart failure (CHF), and coronary heart disease (CHD).\textsuperscript{22} Consistent with the literature, presence of HT, DM and CHD were similar in smokers and non-smokers, while CHF was more frequent in non-smokers in our study.

**LIMITATION**

There are limitations for this study that should be considered. First, it is a retrospective study, and data collection was based on medical records. Second, this was a cross-sectional study, whereas a prospective cohort study is required to evaluate whether differences in lung function decline and treatment responses exist between smokers and non-smokers with COPD.

**CONCLUSION**

COPD is a very complex disease that is widespread all over the world with high mortality and morbidity. Efforts to determine phenotypes are going on due to the wide variety and diversity of patients. Non-smokers with COPD have more biomass exposure, ETS exposure, and infection history in childhood. They also have less impairment of airflow limitation, better symptom scores, higher BMI. Smoking history may be a feature that can be used to determine a different phenotype.

**Ethics Committee Approval:** This study approved by Ethics committee of University of Health Sciences, Dr Suat Seren Chest Diseases and Surgery Research and Training Hospital (Approval No: 2.1.2018/13).
Informed Consent: Verbal informed consent was obtained from the patients and their caregivers who agreed to take part in the study.

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