TANAFFOS

Comparison of Chronic Obstructive Pulmonary Diseases Induced by Wood Smoke and Tobacco Smoke

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Background: Chronic obstructive pulmonary disease (COPD) is a progressive airflow limitation and decline in lung function. Although tobacco smoke is the leading risk factor for COPD, air contamination by wood-burning smoke is also of great concern. About half of the world's populations, especially in developing countries such as Iran, exploit this energy source for cooking and heating. It is remained unknown if COPD induced by wood smoke from baking bread (COPD-B) and COPD induced by tobacco smoke (COPD-S) have different symptoms and clinical presentations. To fill this gap, the present study was to describe such differences.

Materials and Methods: This retrospective cohort study was performed in Afshar COPD clinics affiliated with the Shahid Sadoughi University of Medical Sciences, Yazd, Iran. The clinical records of 231 patients with the COPD diagnosis were reviewed. After considering inclusion and exclusion criteria, 91 patients (46 with COPD-B and 45 with COPD-S) underwent physical examination and para-clinical assessments (i.e., respiratory function tests, Chest X-ray, and quality of life test).

Results: The COPD-B patients were mainly women at older age and had higher FEV_1/FVC and FEF-75; however, they had fewer post-bronchodilator positive responses to FEV_1 (suggesting a restriction pattern) and sputum production, compared to the COPD-S patients. Regarding the other parameters, there were no statistically significant differences between the two groups.

Conclusion: This was the first study evaluating and revealing some differences in the clinical and paraclinical characteristics of the COPD-B patients (with prolonged exposure to wood smoke from bread baking; >100 hours per year, for at least 10 years) and COPD-S patients (>10 packs per year of exposure to tobacco smoke).

Key words: Chronic Obstructive Pulmonary Disease (COPD); Wood smoke; Tobacco smoke; Respiratory function tests; Air pollution; Biomass

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by a persistent, irreversible, and progressive airflow limitation and decline in lung function (1). COPD is a progressive lung disease, which may threaten the life in exacerbated and severe cases by 10% involvement in individuals aged >40 years old. Aging and frequent smoking can increase the rate of its incidence as such the disease is the fourth leading cause of death globally, accounting for about 251 million deaths per year(2). Moreover, this disease is the main cause of chronic morbidity and mortality worldwide

(3). Although tobacco smoke is widely recognized as a main environmental risk factor leading to COPD, the relatively high frequency of the COPD patients in international studies are never-smokers (4). In this regard, there are several risk factors, with air contamination by biomass burning smoke (mainly wood) in enclosed spaces being one of the most important factors (5-10).

Biomass (wood smoke) exposure refers to human inhalation of any gaseous or particulate emissions from biomass (wood) burning (11). About three billion persons (half of the world's population) in different countries, especially in developing countries such as Iran use biomass (mainly wood) as a source of energy at home for cooking and heating (4,8,12,13). Similarly, the use of wood as an "energy saving" measure for heating has also increased in developed countries.

In the rural areas of Yazd, Iran, wood is commonly used for cooking and baking bread. Given the cold weather in winter, people in those areas usually cook inside their houses in poorly ventilated spaces and on stoves without a chimney. This increases household air pollution and is a risk factor for the development of COPD, especially in women (14). There is no report on the prevalence of COPD in this region; however, exposure to wood smoke is the only COPD risk factor detected in many COPD cases from these areas.

It is remained unknown if COPD induced by wood smoke from baking bread (COPD-B) and COPD induced by tobacco smoke (COPD-S) have different symptoms and clinical presentations(15); however, these clinical profiles have recently been described in some studies (13). Although COPD by biomass burning is similar to COPD-S in many aspects, clinical differences are observed. To refer to some of the differences, the COPD-W patients were predominantly female, had less airflow obstruction, and bronchitis was the main phenotype among these patients (16). On the other hand, in the COPD-S cases, the emphysema was the most frequent phenotype and airflow obstruction was more severe (13, 17). However, both groups had similar bronchial symptoms, exercise capacity,

quality of life, healthcare services, and supplemental oxygen.

The present study was to describe and compare the clinical and para-clinical findings in patients with COPD induced by wood smoke from baking bread (COPD-B) and COPD induced by tobacco smoke (COPD-S) (COPD-S).

MATERIALS AND METHODS
Research population and sample

This retrospective cohort study was conducted in the Pulmonology Department of a University Hospital with 1138533 inhabitants (Yazd, Iran, 2016). Many of the patients were from rural areas where wood was commonly used for baking bread. During March 2016-February 2017, 6700 patients attended the Afshar COPD clinics affiliated with the Shahid Sadoughi University of Medical Sciences, Yazd, Iran. The clinical records of 231 patients with the clinical and functional diagnosis of COPD were retrospectively reviewed. The patients were included in the study via phone calls, if they were willing to participate in this study.

Two groups of the COPD patients were formed and compared in this study. The first group of the patients (COPD-B) had COPD secondary to former and/or current exposure to wood smoke, mainly because of baking bread in traditional wood stoves, with no background of active or passive tobacco cigarette smoking. The second group (COPD-S) had COPD secondary to former and/or current exposure to tobacco (cigarette) smoke, with no history of exposure to wood smoke.

Inclusion criteria in this study were as follows: aged >40 years, the COPD diagnosis according to the GOLD 2017 guideline (1), and a history of remarkable exposure to either wood smoke from baking bread (> 10 years, at least twice per week, one hour per time; > 100 hours/year) or tobacco smoke (> 10 packs per year) (18). The level of exposure to wood smoke or tobacco smoke was determined in the interviews.

Cigarette smokers had smoked at least 100 cigarettes in their lifetime. Otherwise, they were considered as never-

smokers. This cumulative tobacco smoking as Pack/years represents the number of cigarettes smoked per day/20 × years of smoking (19).

A brief health questionnaire, including items on chronic diseases, was administered among the participants at this stage (to detect exclusion criteria).

Exclusion criteria were documented or self-reported history of other chronic pulmonary conditions such as alpha-1 antitrypsin deficiency, cystic or cylindrical bronchiectasis attributed to other factors than COPD, lung cancer, interstitial lung diseases, current diagnosis of asthma, and parenchymal lung disease associated with previous tuberculosis (sequelae); human immunodeficiency virus infection; history of exposure to inorganic dust or other types of smoke than those produced by burning tobacco or wood (e.g., water pipe smoke) with a significant amount of tar at workplace; inflammatory diseases; non- Iranian ancestries; and simultaneous exposure to both wood and tobacco smoke (exposure to both risk factors). The patients with COPD were clinically stable and experienced no exacerbation for at least six weeks before the study. Otherwise, they were excluded from this study.

Meeting the inclusion and exclusion criteria, the research sample encompassed 91 patients (46 COPD-B and 45 COPD-S patients). These patients underwent physical examination and para-clinical assessment (Table 1).

All participants who were invited to participate in the study signed an informed written consent document and were provided with a privacy statement describing the confidentiality of their personal information. The study was approved by the Local Research Ethics and Science Committee at the Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Pulse oximetry

Pulse oximetry was performed by a trained technician using Nonin tabletop pulse oximeters (Model 7500, Nonin Medical, Inc., Minnesota, USA).

Respiratory function tests

Spirometry was conducted by a trained technician using Spirolab III spirometer (MIR Corporation, Rome, Italy) in terms of both pre-and post-bronchodilation. The test results were interpreted by authors as monitoring tests, according to the American Thoracic Society and European Respiratory Society guidelines (20, 21). The patients were asked not to smoke during the test day. Spirometry was done in a standing position, and only a forced vital capacity (FVC) maneuver was performed. Each Patient had three to eight spirometry attempts (with a rest period between each phase), of which at least three acceptable maneuvers were finally attained. Global Lung Function Initiative (GLI) reference values were used to calculate the percentage predicted for forced expiratory volume in one second (FEV_1)/FVC, FEV_1, and FVC (22). The ethnic group was considered Oriental (Middle East), treated as Caucasians, and needed no correction.

The COPD diagnosis was confirmed by using pulmonary function tests and applying diagnostic criteria according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 guidelines (1).

Chest X-ray

The chest findings (Table 1) were quantified by a plain radiograph (X-ray) of the chest, in accordance with a previously described method (23).

The images were interpreted independently by two radiologists and one pulmonologist, and experts in the chest plain radiograph (X-ray), who were blinded to the clinical diagnosis groups. Subsequently, the images were read jointly by the three observers blindly to achieve consensus.

Quality of life assessment

The participants' quality of life was assessed by a Persian version of the SF-36 questionnaire (24). The SF-36 is a 36-item scale measuring health status and quality of life with minimum and maximum scores of 0 and 100, respectively.

Table 1. Demographics, Exposure and COPD properties, respiratory and general signs and symptoms, pulmonary Function tests and Chest X-ray findings in COPD-B and COPD-S patients. *

Variable			Patients Groups (n=91)		P-value
			COPD-B n=46, 50.6%	COPD-S n=45, 49.4%	
Demographic	Age, years		69±9.78	64.58 ±10.3	0.039
	Gender	Male (n, %)	1	44, 97.8%	0.001
		Female (n, %)	45, 97.8%	1	0.001
Exposure	Wood burning smoke raised by Baking bread, years		25.12±13.41	0	0.001
	Tobacco Smoking, Pack-Years		0	44.33±20.58	0.001
COPD properties	COPD history, years		4.2±4.37	4.69±5.69	0.681
	Number of COPD exacerbation (leads to hospital admissions) in previous 5 years		0.71±1.44	0.78±1.12	0.827
	Oxygen supplementation (%)		13	11.1	0.853
	Baseline SpO2, %		92.59±4.81	92.86±4.29	0.784
	Quality of life **		49.75±23.72	58.42±24.07	0.163
General and Respiratory signs and Symptoms	Rales on auscultation (%)		13	13.3	0.367
	Wheeze on auscultation (%)		47.8	62.2	0.187
	Cyanosis (%)		4.3	8.9	0.619
	Clubbing (%)		4.3	4.4	0.997
	Edema (%)		13	20	0.667
	Dyspnea (%)		84.8	82.2	0.742
	Wheezing (%)		71.7	75.6	0.68
	Cough (%)		73.9	57.8	0.104
	Sputum (productive cough) (%)		34.8	68.9	0.001
Respiratory function tests	FEV_1, % of predicted		67.16±22.71	62.93±21.23	0.366
	FVC, % of predicted		65.61±20.44	66.89±25.05	0.793
	FEV_1/FVC, %		83.14±13.34	75.56±13.20	0.022
	FEF-25, % of predicted		47.07±23.60	46.60±23.61	0.926
	FEF-75, % of predicted		103.5±56.46	66.29±38.88	0.001
	Low Flow (%)		63	75.6	0.223
	Post-bronchodilator positive response in FEV_1 (%)		34.8	64.4	0.007
Chest X-ray findings	Reticular pattern (%)		63	44.4	0.099
	Over-aeration (%)		32.6	53.3	0.098
	Bronchial thickness (%)		13	24.4	0.246
	Pulmonary artery prominence (%)		28.3	13.3	0.119
	Cardiomegaly (%)		19.6	13.3	0.425

* Values expressed as mean ± SD; except otherwise stated in parenthesis.

** assessed by SF-36 questionnaire. (0-100 scale and 100 is the best score); it was completed for 31 patients in COPD-B and 30 patients in COPD-S group

Parsons's Chi-square statistics was used for non-parametric variables, whereas the independent t-test was used for parametric variables. Two-tailed p-value of <0.05 was considered significant.

COPD-B: COPD related to wood-smoke raised by Baking Bread

COPD-S: COPD related to tobacco Smoking

FEV_1= Forced Expiratory Volume in One second

FVC= Forced Vital Capacity

FEF-25= Forced Expiratory Flow at 25% of the pulmonary volume

FEF-75= Forced Expiratory Flow at 75% of the pulmonary volume

Statistical Analysis

Data analyses were performed using the Statistical Package for Social Sciences (Release 24.0 for Windows, SPSS Inc., Chicago, U.S.). Parsons's Chi-squared test was used for non-parametric variables, whereas the independent-samples t-test was used for parametric variables. Two-tailed p<0.05 was considered as the significance level.

The qualitative (discrete) variables are expressed as proportions (percentage); however, the quantitative variables are described as means ± standard deviations.

Regarding the retrospective nature of some stages of data collection in this study, the sample size was not calculated beforehand.

RESULTS

In this study, 91 patients meeting the study inclusion criteria were evaluated, none of whom were later excluded due to incomplete data. The required data for all parameters were retrieved for all 91 patients included in the analysis (except for the quality of life assessment). In this study, 46 patients (50.6%) were assigned to the COPD-B group, and 45 persons (49.4%) were placed in the COPD-S group. Table 1compare the clinical and para-clinical findings of the two groups.

The patients' ages ranged from 50 to 90 years. The COPD-B group was older than the COPD-S group (69 ± 9.7 vs. 64.5 ± 10.3). In this regard, there was a significant difference between the two groups in terms of age. The COPD-B group also encompassed more women than the COPD-S group (45 female patients (97.8%) vs. one female patient); however, the COPD-S group included more men than the COPD-B group (44 patients (97.8%) vs. one patient).

The COPD-W patients had an average history of 25.1 ± 13.4 years of exposure to wood smoke from baking bread, whereas the mean accumulated tobacco smoking burden in the COPD-S group was 44.3 ± 20.5 packs/year. The patients with COPD-W were nonsmokers, and the COPD-S group had no history of wood smoke exposure.

There was no significant difference between the two groups regarding years of COPD history. Furthermore, hospitalization rates for COPD and oxygen supplementation were also similar in the two groups. Baseline pulse oximeter O_2 saturation (SpO_2) was not significantly different between the two groups (92.59 ± 4.81 in COPD-B patients vs. 92.86 ± 4.29 in COPD-S patients; P=0.784).

The SF-36 questionnaires were completed for 31 and 30 patients in the COPD-B and COPD-S groups, respectively. The other participants failed to complete the questionnaire due to illiteracy or old age; however, the quality of life assessment showed no statistically significant difference between the two groups.

There was no significant difference between the two groups regarding general and respiratory signs and symptoms, except for sputum production, which was more common in the COPD-S group (68.9% vs. 34.8%; $p= 0.001$). Moreover, wheeze on auscultation was more common in the COPD-S patients than the COPD-B patients; however, the difference was not statistically significant (62.2% vs. 47.8%; $p= 0.187$)

All patients had an obstructive pattern. There was no significant difference between the two groups regarding the degree of impairment. No significant difference was observed when FEV_1 and FVC (percentage of predicted value) and FEF-25 (Forced Expiratory Flow at 25% of the pulmonary volume) were compared in the COPD-B and COPD-S groups. There were statistically significant differences between COPD-W and COPD-S in terms of FEV_1/FVC and FEF-75 (Table 1). Post-bronchodilator improvement in the FEV_1 percentage of the predicted value was mainly observed in the COPD-S patients than the COPD-B patients, indicating a statistically significant difference (64.4% vs. 34.8%; $p= 0.007$).

The radiologic findings on chest X-ray showed no statistically significant difference between the two groups regarding any of the examined parameters; however, a reticular pattern was more common in the COPD-B patients, and over-aeration was more common in the COPD-S group.

DISCUSSION

According to the clinical and para-clinical findings, we demonstrated that, unlike patients with COPD-S, a majority of the COPD-B patients were elderly women and had higher levels of FEV_1/FVC and FEF-75; however, they had fewer post-bronchodilator positive responses in FEV_1 (which may suggest a restriction pattern) and sputum production. Regarding the other concerned parameters such as radiographic findings (Last row in Table 1), there was no statistically significant difference between the two groups (Table 1).

The female subjects with COPD-B in this study had the typical clinical and functional characteristics of COPD without a history of tobacco smoking and were a representative sample of the patient population with COPD-B treated in our clinic.

Many scientific articles have been published on COPD; however, few papers have addressed the association between this disease and exposure to biomass smoke, especially wood smoke (25). Furthermore, to the best knowledge of the authors, this study had novelty study as it assessed the patients with COPD exposed to wood smoke from baking bread. The main objective of the present study was to determine whether there were differences in the prevalence of specific clinical and paraclinical characteristics of COPD between the COPD-B and COPD-S patients.

This study revealed some clinical differences between the COPD-S and COPD-B groups. Not surprisingly, the frequency of women in the COPD-B group was much higher since women have traditionally been in charge of baking bread.

The patients in the COPD-B group were significantly older (Table 1, *P* = 0.039), as reported in other studies (13). This finding can be justified from several perspectives. Although exposure to wood smoke generally begins at an early age, it is typically intermittent, and the highest levels of contaminant inhalation are only reached during cooking or baking; thus, damage to the respiratory tract with wood smoke may develop at a slower rate than the less sporadic exposure to tobacco smoke. This finding implies that the harmful effects of wood smoke progress more slowly than those of tobacco smoke due to biological differences of their composition. Accordingly, the COPD with wood smoke from baking bread characteristically needs a longer time to develop than COPD induced by tobacco smoking (26). The diagnosis of COPD-B may also be delayed since there is less information on this association than on tobacco; therefore, patients might be expected to refer at a more advanced stage of the disease. Unlikely, differences may also be influenced by a bias in survival; however, previous studies have indicated similar mortality rates in patients with tobacco- and biomass-induced COPD after correction for possible confounding factors (13). Given the study design, all these hypotheses are merely speculative.

We found less sputum production in the COPD-B group. This finding is consistent with those of some previous studies (27). Furthermore, a study in China revealed that COPD patients with no history of smoking had fewer coughs and sputum production than smokers. However, this article did not directly address COPD induced by biomass smoke (28). In contrast, other studies have documented increased bronchial hyper-responsiveness, coughs, and expectoration in COPD-W patients (29, 30). On the other hand, Ramírez-Venegas et al. reported no difference between the COPD-W and COPD-S groups regarding the percentages of patients with coughs and moderate/severe expectoration (13).

In line with previous studies (13, 31), this study suggested no significant difference between the COPD-B and COPD-S groups in terms of the number of hospital admissions for COPD exacerbations. This finding is of paramount importance since recurrent exacerbations are associated with poor quality of life, accelerated loss of pulmonary function, and higher death rates (32).

This study also aimed to detect the differences in quality of life in the two research groups. This finding is critical due to its connotations for the prognosis. To the best knowledge of the authors, this was the first study assessing and comparing the quality of life (by SF-36

questionnaire) between the COPD-W (or COPD-B) and COPD-S patients. In this regard, the two groups exhibited no significant difference.

This study had several limitations. The most obvious limitation was the inclusion of a relatively small sample number of patients. However, the strict inclusion criteria based on the type of exposure (wood smoke from baking bread or tobacco smoke) and the exclusion of those who were simultaneously exposed to both types of smoking, led to the formation of the two comparable groups, thereby decreasing the likelihood of some overlap between the COPD-B and COPD-S groups. Moreover, patients were recruited from the Pulmonology Department of a hospital; hence, a sampling bias was inevitable. In other words, the research sample cannot be considered as the representative of the whole population. The third limitation was that it was difficult to estimate the exact level of exposure to wood smoke because of the retrospective nature of this assessment and its variation over time.

To sum up, a dose-response relationship could not be established between exposure to smoke and the disease severity and/or comorbidities. Although workplace exposure to inorganic (mineral) dust and other toxic smoke, vapor, or dust was excluded from this study, many of the patients exposed to wood smoke were farmworkers and livestock breeders who, as such, were exposed to organic dust and gases, implying their association with the development of chronic airway limitation (33). This confounding factor, which was observed in previous studies on biomass COPD primarily in rural settings, was difficult to be eliminated. Socioeconomic factors associated with less favorable pulmonary function were another possible confounding factor, which was difficult to be controlled in this population. Finally, recall bias was predicted due to the old age of the included patients.

Despite its limitations, this study detected some differences between COPD-B and COPD-S, demonstrating different biological consequences posed by the two types of smoking.

CONCLUSION

In summary, the COPD-B patients, who developed the disease by their prolonged exposure to wood smoke from baking bread (>100 hours per year, for at least 10 years), were mostly women of older age and had higher FEV_1/FVC and FEF-75. However, they revealed fewer post-bronchodilator positive responses to FEV_1 and sputum production compared to the patients with COPD-S (>10 packs per year of exposure to tobacco smoke). Regarding the other parameters (namely COPD properties, quality of life, respiratory and general signs and symptoms, respiratory function tests, and Chest X-ray findings), there were no statistically significant differences between the two groups.

To the best of our knowledge, this research was the first study evaluating the clinical and paraclinical characteristics of the COPD-B patients and comparing them with those of the COPD-S patients. Accordingly, the present study provides the required information for further studies on the same issue.

REFERENCES

1. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global Strategy for the Diagnosis,

Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. *Am J Respir Crit Care Med* 2017;195(5):557-82.

2. Varmaghani M, Farzadfar F, Sharifi F, Rashidian A, Moin M, Moradi-Lakeh M, et al. Prevalence of Asthma, COPD, and Chronic Bronchitis in Iran: A Systematic Review and Meta-analysis. *Iran J Allergy Asthma Immunol* 2016;15(2):93-104.

3. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: current burden and future projections. *Eur Respir J* 2006;27(2):397-412.

4. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009;374(9691):733-43.

5. Sezer H, Akkurt I, Guler N, Marakoğlu K, Berk S. A case-control study on the effect of exposure to different substances on the development of COPD. *Ann Epidemiol* 2006;16(1):59-62.

6. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176(6):532-55.

7. Nardini S, Annesi-Maesano I, Del Donno M, Delucchi M, Bettoncelli G, Lamberti V, et al. The AIMAR recommendations for early diagnosis of chronic obstructive respiratory disease based on the WHO/GARD model*. *Multidiscip Respir Med* 2014;9(1):46.

8. Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. *Proc Am Thorac Soc* 2008;5(5):577-90.

9. Hu G, Zhou Y, Tian J, Yao W, Li J, Li B, et al. Risk of COPD from exposure to biomass smoke: a metaanalysis. *Chest* 2010;138(1):20-31.

10. da Silva LF, Saldiva SR, Saldiva PH, Dolhnikoff M; Bandeira Científica Project. Impaired lung function in individuals chronically exposed to biomass combustion. *Environ Res* 2012;112:111-7.

11. Morandi MT, Ward TJ; Risk Assessment Workgroup. Wood smoke risk assessment: defining the questions. *Inhal Toxicol* 2010;22(2):94-8.

12. Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. *Thorax* 2010;65(3):221-8.

13. Ramírez-Venegas A, Sansores RH, Pérez-Padilla R, Regalado J, Velázquez A, Sánchez C, et al. Survival of patients with chronic obstructive pulmonary disease due to biomass smoke and tobacco. *Am J Respir Crit Care Med* 2006;173(4):393-7.

14. Golshan M, Faghihi M, Marandi MM. Indoor women jobs and pulmonary risks in rural areas of Isfahan, Iran, 2000. *Respir Med* 2002;96(6):382-8.

15. Salvi S, Barnes PJ. Is exposure to biomass smoke the biggest risk factor for COPD globally? *Chest* 2010;138(1):3-6.

16. Ramírez-Venegas A, Sansores RH, Quintana-Carrillo RH, Velázquez-Uncal M, Hernandez-Zenteno RJ, Sánchez-Romero C, et al. FEV1 decline in patients with chronic obstructive pulmonary disease associated with biomass exposure. Am *J Respir Crit Care Med* 2014;190(9):996-1002.

17. Rivera RM, Cosio MG, Ghezzo H, Salazar M, Pérez-Padilla R. Comparison of lung morphology in COPD secondary to cigarette and biomass smoke. *Int J Tuberc Lung Dis* 2008;12(8):972-7.

18. Caballero A, Torres-Duque CA, Jaramillo C, Bolívar F, Sanabria F, Osorio P, et al. Prevalence of COPD in five Colombian cities situated at low, medium, and high altitude (PREPOCOL study). *Chest* 2008;133(2):343-9.

19. Shahab L, Beard E, Brown J. Association of initial e-cigarette and other tobacco product use with subsequent cigarette smoking in adolescents: a cross-sectional, matched control study. *Tob Control* 2021;30(2):212-20.

20. Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, Lundberg JO, et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. *Am J Respir Crit Care Med* 2011;184(5):602-15.

21. Redlich CA, Tarlo SM, Hankinson JL, Townsend MC, Eschenbacher WL, Von Essen SG, et al. Official American Thoracic Society technical standards: spirometry in the occupational setting. *Am J Respir Crit Care Med* 2014;189(8):983-93.

22. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012;40(6):1324-43.

23. Collins J, Stern EJ, editors. Chest radiology: the essentials. Lippincott Williams & Wilkins; 2008.

24. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.

25. Golpe R, Sanjuán López P, Cano Jiménez E, Castro Añón O, Pérez de Llano LA. Distribution of clinical phenotypes in patients with chronic obstructive pulmonary disease caused by biomass and tobacco smoke. *Arch Bronconeumol* 2014;50(8):318-24.

26. Naeher LP, Brauer M, Lipsett M, Zelikoff JT, Simpson CD, Koenig JQ, et al. Woodsmoke health effects: a review. *Inhal Toxicol* 2007;19(1):67-106.

27. Moreira MA, Moraes MR, Silva DG, Pinheiro TF, Vasconcelos Júnior HM, Maia LF, et al. Comparative study of respiratory symptoms and lung function alterations in patients with chronic obstructive pulmonary disease related to the exposure to wood and tobacco smoke. *J Bras Pneumol* 2008;34(9):667-74.

28. Zhou Y, Wang C, Yao W, Chen P, Kang J, Huang S, et al. COPD in Chinese nonsmokers. *Eur Respir J* 2009;33(3):509-18.

29. González-García M, Torres-Duque CA, Bustos A, Jaramillo C, Maldonado D. Bronchial hyperresponsiveness in women with chronic obstructive pulmonary disease related to wood smoke. *Int J Chron Obstruct Pulmon Dis* 2012;7:367-73.

30. González-García M, Maldonado Gomez D, Torres-Duque CA, Barrero M, Jaramillo Villegas C, Pérez JM, et al. Tomographic and functional findings in severe COPD: comparison between the wood smoke-related and smoking-related disease. *J Bras Pneumol* 2013;39(2):147-54.

31. Golpe R, Sanjuán López P, Cano Jiménez E, Castro Añón O, Pérez de Llano LA. Distribution of clinical phenotypes in patients with chronic obstructive pulmonary disease caused by biomass and tobacco smoke. *Arch Bronconeumol* 2014;50(8):318-24.

32. Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005;60(11):925-31.

33. Eduard W, Pearce N, Douwes J. Chronic bronchitis, COPD, and lung function in farmers: the role of biological agents. *Chest* 2009;136(3):716-25.