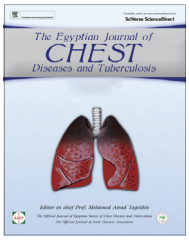
Egyptian Journal of Chest Diseases and Tuberculosis (2012) **61**, 59–65

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

www.elsevier.com/locate/ejcdt
www.sciencedirect.com



ORIGINAL ARTICLE

Prevalence characteristics of COPD in never smokers

Ramadan M. Bakr *, Ibrahim I. Elmahallawy

Chest Department, Menoufiya University, Egypt

Received 7 June 2012; accepted 17 June 2012
Available online 30 January 2013

KEYWORDS

Chronic obstructive pulmonary disease (COPD);
Ever smokers;
Never smokers;
Environmental tobacco smoke (ETS);
Global Initiative for Obstructive Lung Disease (GOLD)

Abstract *Background:* Chronic obstructive pulmonary disease (COPD) is currently the 4th leading cause of death all over the world. Smoking is by far the most important documented (and preventable) cause for COPD. However, COPD can still be recorded among a good percentage of non smoker patients, due to other different causes.

Methods: This study was performed in the Chest Department, Menoufiya University, in the period from April 2009 to August 2011, on randomly selected 300 COPD patients, 230 patients (76.66%) were men and 70 patients (23.34%) were women. The mean age of the patients was 60.7 ± 5.35 years (range 42–83 years), and all patients were diagnosed as having COPD (FEV_1/FVC < 70%), with the use of spirometry (prebronchodilator and postbronchodilator inhalation), according to the GOLD criteria. For each patient, the personal history (including his or her education level), smoking history, health status, and exposure to risk factors for COPD, were assessed according to a prewritten questionnaire.

Results: Out of the 300 COPD patients included in this study, 120 (40%) were never smokers and 180 (60%) were ever smokers. Women made up 41.7% of the never smokers (50 of 120) and 11% of the ever smokers (20 of 180). Never smokers were significantly older than smokers [65.08 ± 5.03 years vs 56.33 ± 5.67 years ($P < 0.001$)] and were more likely to be women [41.7% vs 11% ($P < 0.001$)]. Never smokers made up to 40% (120/300) of all COPD cases: 78% (70/90) of all GOLD stage II cases, 45.5% (50/110) of all GOLD stage III cases. Among never smokers, 58.3% (70/120) fulfilled the criteria for GOLD stage II and 41.7% (50/120) fulfilled the criteria for GOLD stage III and no patients fulfilled the criteria of either GOLD stage I or GOLD stage IV. Never smokers were shown to have more occupational exposure to organic and inorganic dust and irritant gases at work place [41.7% (50/120) vs 27.7% (50/180), $P < 0.05$], more biomass exposure [41.7% (50/120) vs 0% (0/180), $P < 0.001$], less education [41.7% (50/120) vs 72.2% (130/180), $P < 0.001$], more exposure to passive smoking [75% (90/120) vs 22.2% (40/180), $P < 0.001$]. When compared with never smoker patients with moderate COPD (GOLD stage II), never smokers

* Corresponding author. Address: Chest Department, Menoufiya University, Shebin Elkom, Egypt. Mobile: +20 1005290101.
E-mail address: ramadanbakr65@yahoo.com (R.M. Bakr).

Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

ELSEVIER Production and hosting by Elsevier

 http://dx.doi.org/10.1016/j.ejcdt.2012.10.035

with severe COPD (GOLD stage III) were older in age (70.6 ± 2.44 years vs 61.14 ± 1.25 years, $P < 0.001$), have a higher female percentage (60% vs 28.6%, $P < 0.001$), lower BMI (21.2 ± 0.76 vs 26.14 ± 2.43, $P < 0.001$), more occupational exposure (27.5 ± 2.56 years vs 13.33 ± 2.39 years, $P < 0.001$), more biomass exposure (35 ± 4.15 years vs 20 ± 10 years, $P < 0.001$), less education (0% vs 71.4 educated, $P < 0.001$), more exposure to passive smoking (29 ± 2.02 years vs 13.75 ± 4.19 years, $P < 0.001$).

Conclusions: This study revealed that never smokers constitute a significant proportion of the Egyptian COPD patients. When dealing with COPD management, clinicians must be oriented with the different risk factors, other than tobacco smoke, that play a key role in the development and pathogenesis of COPD, because despite smoking is the most important risk factor, its absence doesn't exclude COPD diagnosis.

Introduction

Chronic obstructive pulmonary disease (COPD) is an important and increasing cause of morbidity and mortality worldwide. It is the fourth leading cause of death and is projected to rank third among all causes of death by 2020 [1].

Smoking is by far the major cause of COPD worldwide, a fact that has been well known for at least 2 decades. COPD is considered rare in persons with no smoking history except in the context of another exposure, such as occupational dust, environmental air pollution, or biomass fuel. Accordingly, the disease has not been well characterized in persons who have never smoked [2–4].

However, in the past decade and especially the past 5 years, results from a growing number of published studies have suggested that risk factors other than smoking are strongly associated with COPD. These factors include exposure to indoor and outdoor air pollutants, workplace exposure to dust and fumes, history of repeated lower respiratory-tract infections during childhood, history of pulmonary tuberculosis, chronic bronchial asthma, intrauterine growth retardation, poor nourishment, and poor socioeconomic status [5]. It is now recognized that never smokers may account for between one-fourth and one-third of all COPD cases [6].

Patients and methods

The study was conducted on randomly chosen 300 COPD patients aged from 42 to 83 years (60.7 ± 5.35) and (230 men and 70 women) during their admission in the Chest Department, Menoufiya University Hospitals or during their follow up visits to the outpatient clinic of the same, from April 2009 to August 2011. A written consent was obtained from each patient participating in this study.

All participants included in the study performed prebronchodilator and postbronchodilator spirometry and recorded a questionnaire data on personal history, smoking history, health status, and exposure to risk factors for COPD.

Spirometry

Spirometry was performed according to American Thoracic Society (ATS) criteria [7]. Separate measurements were made before and at least 15 min after two puffs of Salbutamol (200 mg) administered with a metered dose inhaler with volumatic spacer. Irreversible airway obstruction was defined as a postbronchodilator FEV1/FVC < 0.7 according to the GOLD (Global Initiative for Obstructive Lung Disease) guidelines and the FEV1 was used to further stage the disease: FEV1 < 80% predicted served as the threshold for GOLD stage II COPD, FEV1 < 50% predicted served as the threshold for GOLD stage III COPD and FEV1 < 30% predicted served as the threshold for GOLD stage IV COPD [8].

Questionnaire data

Questionnaire data were obtained from each patient and included information on smoking history and risk factors for COPD, education, comorbidities, respiratory diagnoses and childhood diseases.

An ever smoker (current or former) was defined as a person who had smoked >20 packs of cigarettes in a lifetime or >1 cigarette/d for a year. Exposure to passive cigarette smoke was defined as an answer to whether anyone (other than the participant) had smoked a cigarette, pipe, cigar or shisha in the participant's home or workplace. To assess occupational exposure, participants were asked whether they had worked >3 months in occupations known or suspected to be associated with the risk of COPD and, if so, the number of years spent in each occupation. Occupational exposures were grouped into three categories: organic dust, inorganic dust and irritant gases, fumes, or vapors. Biomass exposure was recorded if the participant had experienced at least 6 months use of indoor fire for cooking or heating. Participants also reported the number of years of biomass exposure.

Additional measures evaluated included body mass index [BMI (kg/m^2)]; total number of years of education; self-reported hospitalizations for respiratory problems prior to the age of 10 years; and self-reported physician-diagnosed bronchial asthma, COPD, chronic bronchitis, emphysema or TB.

Results

A total of 300 COPD patients had acceptable postbronchodilator spirometry data and completed the questionnaires. Of this group, 120 (40%) were never smokers and 180 (60%) were smokers. Women made up 41.7% of never smokers (50 of 120) and 11% of ever smokers (20 of 180).

Characteristics of the study population in smokers and never smokers are summarized in Table 1. Never smokers were significantly older than smokers [65.08 ± 5.03 years vs 56.33 ± 5.67 years ($P < 0.001$)] and were more likely to be

Table 1 Population characteristics in smokers and never smokers.

	Never Smokers (n = 120)		Smokers (n = 180)		X^2	P value
	No (%)		No (%)			
Age; years (mean ± SD)	65.08 ± 5.03		56.33 ± 5.67		13.69*	< 0.001
Sex						
Males, No (%)	70	58.3	160	89	37.58	< 0.001
Females, No (%)	50	41.7	20	11		
BMI; kg/m^2 (mean ± SD)	24.08 ± 3.11		25.28 ± 4.45		2.51*	< 0.05
FEV1/FVC (mean ± SD)	57.83 ± 4.41		47 ± 8.38		13*	< 0.001
FEV1% (mean ± SD)	50.33 ± 7.38		36.17 ± 8.04		15.45*	< 0.001
FEV1 < 80% ⩾50% predicted (GOLD stage II)	70	58.3	20	11.1	76.46	< 0.001
FEV1 < 50% >30% predicted (GOLD stage III)	50	41.7	60	33.3	2.15	> 0.05
FEV1 ⩽ 30% predicted (GOLD stage IV)	0	0	100	55.6	100	< 0.001
Occupational exposure						
Yes	50	41.7	50	27.8	6.25	< 0.05
No	70	58.3	130	72.2		
Biomass exposure						
Yes	50	41.7	0	0	90	< 0.001
No	70	58.3	180	100		
Education						
Yes	50	41.7	130	72.2	28.01	< 0.001
No	70	58.3	50	27.8		
Passive smoking						
Yes	90	75	40	22.2	81.67	< 0.001
No	30	25	140	77.8		
Physician diagnosed chest disease						
Yes	70	58.3	150	83.3		
No	50	41.7	30	16.7	23.01	< 0.001
Childhood hospitalization						
Yes	40	33.3	20	11	22.22	< 0.001
No	80	66.7	160	89		

* t Test.

women [41.7% vs 11% (P < 0.001)]. Never smokers made up to 40% (120/300) of all COPD cases: 78% (70/90) of all GOLD stage II cases, 45.5% (50/110) of all GOLD stage III cases. Among overall never smokers, 58.3% (70/120) fulfilled the criteria for GOLD stage II and 41.7% (50/120) fulfilled the criteria for GOLD stage III. No patients among this group fulfilled the criteria of either GOLD stage I or GOLD stage IV. Never smokers had higher FEV1/FVC ratio [57.83 ± 4.41 vs 47 ± 8.38 (P < 0.001)], higher FEV1% [50.33 ± 7.38 vs 36.17 ± 8.04 (P < 0.001)] and lower BMI [24.08 ± 3.11 vs 25.28 ± 4.45 (P < 0.05)] than ever smokers.

Never smokers reported more occupational exposure to organic and inorganic dust and irritant gases at work place [41.7% (50/120) vs 27.7% (50/180), P < 0.05], more biomass exposure [41.7% (50/120) vs 0% (0/180), P < 0.001], less education [41.7% (50/120) vs 72.2% (130/180), P < 0.001], more exposure to passive smoking [75% (90/120) vs 22.2% (40/180), P < 0.001], less physician diagnosed chest disease [58.3% (70/120) vs 83.3% (150/180), P < 0.001] and more hospitalization due to respiratory problems during childhood [33.3% (40/120) vs 11% (20/180), P < 0.001] than smokers (Table 1).

Among never smokers, Table 2 compares between patients with moderate COPD (GOLD stage II) and those with severe COPD (GOLD stage III) regarding the demographic data and exposure to different risk factors. Table 2 shows that never smokers with severe COPD (GOLD stage III) were older in age (70.6 ± 2.44 years vs 61.14 ± 1.25 years, P < 0.001), have a higher female percentage (60% vs 28.6%, P < 0.001), lower BMI (21.2 ± 0.76 vs 26.14 ± 2.43, P < 0.001), more occupational exposure (27.5 ± 2.56 years vs 13.33 ± 2.39 years, P < 0.001), more biomass exposure (35 ± 4.15 years vs 20 ± 10 years, P < 0.001), less education (0% vs 71.4 educated, P < 0.001), more exposure to passive smoking (29 ± 2.02 years vs 13.75 ± 4.19 years, P < 0.001), higher percentage of physician diagnosed chest diseases (80% vs 42.85%, P < 0.001) and more childhood hospitalizations (80% vs 0%, P < 0.001) than never smokers with moderate COPD (GOLD stage II).

Table 3 shows an association between increasing age and increasing odds of COPD severity (OR = 2.1 and P < 0.05 for ages from 50 to 59 years and OR = 2.7 and P < 0.05 for ages from 60 to 75 years). There was also an association between female sex and COPD severity in never smokers (OR = 1.9 and P < 0.05). Occupational exposure and biomass exposure were significantly associated with the occurrence and severity of COPD among never smokers (OR = 1.09 and P < 0.05 and OR = 1.26 and P < 0.05 respectively). The table shows also an association between education less than 9 years and increasing odds of COPD severity (OR = 0.96 and P < 0.05).

Table 2 Population characteristics among never smokers according to the GOLD stage.

Characteristic	GOLD II (n = 70)		GOLD III (n = 50)		t Test	P value
Age; years (mean ± SD)	61.14 ± 1.25		70.6 ± 2.44		27.72	< 0.001
Sex						
Males, No (%)	50	71.4	20	40	11.85	< 0.001
Females, No (%)	20	28.6	30	60		
BMI; kg/m^2 (mean ± SD)	26.14 ± 2.43		21.2 ± 0.76		13.88	< 0.001
Occupational exposure; years (mean ± SD)	13.33 ± 2.39 (n = 30)		27.5 ± 2.56 (n = 20)		19.91	< 0.001
Biomass exposure; years (mean ± SD)	20 ± 10 (n = 20)		35 ± 4.15 (n = 30)		16.1	< 0.001
Education						
−ve	20(28.6)		50(100)		61.22*	< 0.001
+ve	50(71.4)		0(0)			
Passive smoking; years (mean ± SD)	13.75 ± 4.19 (n = 40)		29 ± 2.02 (n = 50)		22.64	< 0.001
Physician diagnosed chest disease; No (%)	30	42.85	40	80	16.56	< 0.001
Childhood hospitalization; No (%)	0	0	40	80	84	< 0.001

* t Test.

No significant association was found between the severity of COPD in never smokers and any of the following predictors: BMI (OR = 0.36 and $P > 0.05$ for BMI between 25 and 30 kg/m^2 and OR = 0.32 and $P > 0.05$ for BMI ⩾ 30 kg/m^2), exposure to passive smoking (OR = 0.22 and $P > 0.05$), physician diagnosed chest disease (OR = 0.43 and $P > 0.05$) and hospitalization due to respiratory problems prior to the age of 10 years (OR = 1.01 and $P > 0.05$).

Table 3 Multivariate logistic analysis of independent predictors of COPD severity among never smokers.

Characteristic	OR	P value	95% CI
Age in years			
40–49	Reference		
50–59	2.1	< 0.05	1.02–1.93
60–75	2.7	< 0.05	1.13–2.3
Sex			
Males	Reference		
Females	1.9	< 0.05	1.4–1.26
BMI, kg/m^2			
20 ⩽ BMI □ 25	Reference		
25 ⩽ BMI □ 30	0.36	> 0.05	0.38–1.61
BMI ⩾ 30	0.32	> 0.05	0.29–1.5
Occupational exposure			
Not exposed	Reference	< 0.05	0.41–0.78
Exposed	1.09		
Biomass exposure			
Not exposed	Reference		
Exposed	1.26	< 0.05	0.38–0.82
Education (years)			
⩾9 years	Reference	< 0.05	0.72–0.8
<9 years	0.96		
Passive smoking			
Not exposed	Reference		
Exposed	0.22	> 0.05	0.82–1.05
Physician diagnosed chest disease			
No	Reference		
Yes	0.43	> 0.05	0.73–1.62
Childhood hospitalization			
No	Reference		
Yes	1.01	> 0.05	0.9–1.93

Discussion

This study shows that 40% of the included COPD patients were never smokers (120/300). Never smokers constituted 78% (70/90) of all GOLD stage II cases, 45.5% (50/110) of all GOLD stage III cases. These findings coincide with those reported by Zhou et al. [9] who studied the prevalence of COPD in Chinese nonsmokers; they found that 38.6% of COPD patients were never smokers. Also, Lamprecht et al. [10] found that 28% of irreversible airways obstruction—about 33% of mild airway obstruction (GOLD stage I) and about 23% of moderate to very severe airway obstruction (GOLD stage II+) occurs in never smokers aged 40–98 years. In agreement with our results, an analysis of (prebronchodilator) NHANES III (National Health and Nutrition Examination Survey) data in US adults (aged 18–80 years), Behrendt CE showed that about one fourth of COPD cases occurred in subjects with no smoking history [11]. Bridevaux et al. [12] studied the prevalence of airflow obstruction in smokers and never-smokers in Switzerland and reported that never smokers constituted 29.3% of subjects with airflow obstruction.

Higher percentage of prevalence was found by Brashier et al. [13] who stated that the proportion of COPD patients who never smoked among 12055 participants above 45 years in India was 68.6%. Also, Ehrlich et al. [14] reported that never smokers made up 47.6% of patients with airway obstruction among 13826 adults in South Africa aged more than 18 years. In both studies, a respiratory symptoms questionnaire was used to define airway obstruction.

On the other hand, lower percentages of prevalence were reported by other authors. Celli BR and colleagues [15] suggested some degree of airway obstruction in 91.2 per 1000 of

US never smokers aged more than 30 years. Mannino and colleagues [16] reported rates of "low lung function" in never smokers ranging from 26 to 48 per 1000. Meyer and colleagues reported that 16.7% of adults who died with COPD had never smoked [17].

These results suggest that nonsmokers represent a significant proportion of obstructive lung disease in different sites of the world. This variation among different rates of prevalence may be attributed to several factors including the exposure to different local risk factors among different countries, the variations among the populations studied regarding the demographic data like age, gender and ethnicity, and the differences in the definitions of low lung function or airway obstruction and the methods used to demonstrate it in different studies.

In the present study, never smokers were significantly older than smokers (65.08 ± 5.03 years vs 56.33 ± 5.67 years, $P < 0.001$), never smokers with severe COPD (GOLD stage III) were older in age (70.6 ± 2.44 years vs 61.14 ± 1.25 years, $P < 0.001$) than never smokers with moderate COPD (GOLD stage II) and we found an association between increasing age and COPD severity (OR = 2.1 and $P < 0.05$ for ages from 50 to 59 years and OR = 2.7and $P < 0.05$ for ages from 60 to 75 years).

These results are consistent with those reported by Lamprecht et al. [10] that showed a strong association between increasing age and increasing odds of GOLD stage II + COPD. Also, Celli et al. [15] concluded that the prevalence of airflow obstruction appeared to increase with age.

Our results showed that never smokers were more likely to be women (41.7% vs 11%, $P < 0.001$) than ever smokers. Table 2 shows that never smokers with severe COPD (GOLD stage III) have a higher female percentage (60% vs 28.6%, $P < 0.001$) than never smokers with moderate COPD (GOLD stage II). There was an association between female sex and COPD severity in never smokers (OR = 1.9 and $P < 0.05$). Corresponding results were reported by many authors as Miravitlles et al. [18], Xu et al. [19], Silverman et al. [20], Dransfield et al. [21], Zhou et al [9], Lamprecht et al. [10] and Bridevaux et al. [12]. They found that the majority of nonsmoking COPD patients were females with a strong association between female sex and COPD severity in never smokers.

Occupational airborne dust is the best documented risk factor for development of COPD after smoking [15], with several studies showing independent associations with decreased lung function in nonsmokers among specific occupational groups [22–24], and in the general population [25,26]. In 2003, results of a systematic epidemiological review into occupational factors associated with COPD by the American Thoracic Society (ATS), showed that about 10% to 20% of both symptoms and functional impairment consistent with COPD might be attributable to workplace exposure [27] and a subsequent follow-up provided similar estimates [28]. Our data confirmed this finding by showing that never smokers reported more occupational exposure to organic and inorganic dust and irritant gases at work place (41.7% vs 27.7%, $P < 0.05$) than ever smokers. Also, never smokers with severe COPD (GOLD stage III) had more years of occupational exposure (27.5 ± 2.56 years vs 13.33 ± 2.39 years, $P < 0.001$) than never smokers with moderate COPD (GOLD stage II). Lastly, occupational exposure was an independent predictor of COPD and was significantly associated with the severity of COPD among never smokers (OR = 1.09 and $P < 0.05$).

Coinciding with our results, Hnizdo and colleagues [29] confirmed the adverse effects of occupational exposures in an analysis of NHANES III data and attributed 31.1% of COPD in never smokers to these exposures. Also, Behrendt CE [11] identified several occupations that were associated with high prevalence of COPD: plastic, textile, rubber, and leather manufacture; transportation; manufacture of food products; automotive repair; and some personal services (e.g., beauty care). The proportion of patients with COPD attributable to occupation was about 19% overall and 31% in never-smokers. Weinmann et al. [30] reported increased prevalence of COPD in occupations associated with chronic exposure to diesel exhaust (e.g., garages and mines) and other irritant gases and vapors. Trupin et al. [31] found a population-attributable fraction for COPD associated with occupational exposure varying between 9% and 31%. Lamprecht et al. [10] postulated that never smokers with moderate to severe COPD reported exposure to organic dusts in the workplace more often than did never smokers with unobstructed airways (30.4% vs 23%).

Worldwide, about 50% of all households and 90% of rural households use biomass fuel (wood, charcoal, other vegetable matter, and animal dung) and coal as their main source of domestic energy. About 3 billion people worldwide are exposed to smoke from biomass fuel compared with 1.01 billion people who smoke tobacco, suggesting that exposure to biomass smoke is one of the most important global risk factors for COPD. About 50% of deaths from COPD in developing countries are attributable to biomass smoke [32,33].

Our results showed that never smokers reported more biomass exposure (41.7% vs 0%, $P < 0.001$) than smokers and never smokers with severe COPD (GOLD stage III) reported more years of biomass exposure (35 ± 4.15 years vs 20 ± 10 years, $P < 0.001$) than never smokers with moderate COPD (GOLD stage II). Biomass exposure was significantly associated with the occurrence and severity of COPD among never smokers (OR = 1.26 and $P < 0.05$).

These findings were consistent with those reported by Smith KR [34], Chan-Yeung et al. [35], Ezzati [36], Oroczo-Levi et al. [37], Ekici et al. [38], Ramírez-Venegas et al. [39] and Lamprecht et al. [10]; all of them found an association between the development of COPD in never smokers and biomass exposure and reported it as an independent predictor of COPD among never smokers.

Regarding the level of education, never smokers reported less education (41.7% vs 72.2%, $P < 0.001$) than smokers. Never smokers with severe COPD (GOLD stage III) have less education (0% vs 71.4 educated, $P < 0.001$) than never smokers with moderate COPD (GOLD stage II). Also, there is an association between education less than 9 years and increasing odds of COPD severity (OR = 0.96 and $P < 0.05$).

These results agree with those found by Nizankowska-Mogilnicka et al. [40] who postulated that low level of education has been shown to be associated with a higher prevalence of COPD. Also, in agreement with our data, Lamprecht et al. [10] reported that more years of education was associated with lower odds of spirometrically determined COPD among female never smokers.

In the present study, although no significant association was found between the severity of COPD in never smokers and exposure to passive smoking (OR = 0.22 and $P > 0.05$), never smokers reported more exposure to passive smoking (75% vs 22.2%, $P < 0.001$) than smokers and never smokers

with severe COPD (GOLD stage III) reported more years of exposure to passive smoking (29 ± 2.02 years vs 13.75 ± 4.19 years, $P < 0.001$) than those with moderate COPD (GOLD stage II).

By reviewing the results of other studies, Yin et al. [41], Eisner et al. [42], Simoni et al. [43], Iribarren et al. [44] and Larsson et al. [45] reported that exposure to environmental tobacco smoke (ETS) is associated with COPD. Lamprecht [10] did not observe an increased risk of GOLD stage II + COPD associated with exposure to passive smoking and Celli BR [15] found a nonsignificant decrease in the odds of obstruction among never smokers who reported exposure to environmental tobacco smoke.

As regards the BMI, it has been recognized as a prognostic factor and a predictor of death in COPD [46] and has shown an association with bronchial hyperresponsiveness [47]. Our data showed that never smokers had lower BMI (24.08 ± 3.11 vs 25.28 ± 4.45 $P < 0.05$) than ever smokers, and never smokers with severe COPD (GOLD stage III) had lower BMI (21.2 ± 0.76 vs 26.14 ± 2.43, $P < 0.001$), than never smokers with moderate COPD (GOLD stage II). No significant association was found between the severity of COPD in never smokers and BMI (OR = 0.36 and $P > 0.05$ for BMI between 25 and 30 kg/m^2 and OR = 0.32 and $P > 0.05$ for BMI $\geqslant$ 30 kg/m^2). Celli et al. [15] found an increased likelihood of obstruction in those with lower BMI and Lamprecht et al. [10] reported increased odds of GOLD stage in the never smoker population with low BMI (< 20 kg/m^2).

Never smokers reported less physician diagnosed chest disease (58.3% vs 83.3%, $P < 0.001$) and more hospitalizations due to respiratory problems during childhood (33.3% vs 11%, $P < 0.001$) than smokers. Also, never smokers with GOLD stage III COPD reported a higher percentage of physician diagnosed chest diseases (80% vs 42.85%, $P < 0.001$) and more childhood hospitalizations (80% vs 0%, $P < 0.001$) than never smokers with moderate COPD (GOLD stage II).

No significant association was found between the severity of COPD in never smokers and either physician diagnosed chest disease (OR = 0.43 and $P > 0.05$) or hospitalization due to respiratory problems prior to the age of 10 years (OR = 1.01 and $P > 0.05$). Lamprecht et al. [10] reported that 81.2% of never smokers with moderate to severe airway obstruction were previously undiagnosed. Also, they found that severe childhood respiratory infections or other breathing problems (leading to hospitalization) and COPD were associated in never smokers. Berglund et al. [48] reported an association between COPD in never smokers and history of childhood disease. Silva et al. [49], Ulrik CS and Lange P [50], Abhyankar and Salvi [51] and Celli et al. [15] found an association between COPD and physician diagnosed chronic chest diseases especially bronchial asthma. Ehrlich et al. [14] suggested an association between COPD and history of pulmonary tuberculosis.

Conclusion

This study revealed that never smokers constitute a substantial proportion of COPD patients. Multiple risk factors, other than tobacco smoke, play a key role in the development and pathogenesis of COPD as increasing age, female gender, exposure to occupational irritants, exposure to biomass fuels, as occurring in Egyptian village inhabitants, low educational level, exposure to environmental tobacco smoke, low BMI, history of childhood chest diseases and history of physician diagnosed chronic chest diseases.

References

[1] C.J. Murray, A.D. Lopez, Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study, Lancet 349 (9064) (1997) 1498–1504.
[2] A.D. Oxman, D.C. Muir, H.S. Shannon, S.R. Stock, E. Hnizdo, H.J. Lange, Occupational dust exposure and chronic obstructive pulmonary disease. A systematic overview of the evidence, Am. Rev. Respir. Dis. 148 (1993) 38–48.
[3] C.A. Pope, D.V. Bates, M.E. Raizenne, Health effects of particulate air pollution: time for reassessment?, Environ Health Perspect. 103 (1995) 472–480.
[4] B.H. Chen, C.J. Hong, M.R. Pandey, K.R. Smith, Indoor air pollution in five developing countries, World Health Stat. Q. 43 (1990) 127–138.
[5] Sundeep S. Salvi, Peter J. Barnes, Chronic obstructive pulmonary disease in non-smokers, Lancet 374 (2009) 733–743.
[6] B. Lamprecht, L. Schirnhofer, B. Kaiser, S. Buist, M. Studnicka, Non-reversible airway obstruction in never smokers: results from the Austrian BOLD study, Respir. Med. 102 (12) (2008) 1833–1838.
[7] American Thoracic SocietyStandardization of spirometry, 1994 update, Am. J. Respir. Crit. Care Med. 152 (3) (1995) 1107–1136.
[8] K.F. Rabe, S. Hurd, A. Anzueto, et al., Global initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary, Am. J. Respir. Crit. Care Med. 176 (6) (2007) 532–555.
[9] Y. Zhou, C. Wang, W. Yao, et al., COPD in Chinese nonsmokers, Eur. Respir. J. 33 (3) (2009) 509–518.
[10] B. Lamprecht, M.A. McBurnie, W.M. Vollmer, et al., COPD in never smokers, results from the population-based burden of obstructive lung disease (BOLD) study, Chest 139 (2011) 752–763.
[11] C.E. Behrendt, Mild and moderate-to-severe COPD in nonsmokers: distinct demographic profiles, Chest 128 (3) (2005) 1239–1244.
[12] P.O. Bridevaux, N.M. Probst-Hensch, C. Schindler, et al., Prevalence of airflow obstruction in smokers and never smokers in Switzerland, Eur. Respir. J. 36 (6) (2010) 1259–1269.
[13] B. Brashier, S. Gangavane, S. Valsa, et al., Almost half the patients treated for pulmonary tuberculosis (TB) show evidence of obstructive airways disease (OAD), in: European Respiratory Society Annual Congress, Stockholm, Sweden; September 15–19, 2007. Abstr. E2585.
[14] R.I. Ehrlich, N. White, R. Norman, et al., Predictors of chronic bronchitis in South African adults, Int. J. Tuberc. Lung Dis. 8 (2004) 369–376.
[15] B.R. Celli, R.J. Halbert, R.J. Nordyke, B. Schau, Airway obstruction in never smokers: results from the Third National Health and Nutrition Examination Survey, Am. J. Med. 118 (12) (2005) 1364–1372.
[16] D.M. Mannino, R.C. Gagnon, T.L. Petty, E. Lydick, Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Survey, 1988–1994, Arch. Intern. Med. 160 (2000) 1683–1689.
[17] P.A. Meyer, D.M. Mannino, S.C. Redd, D.R. Olson, Characteristics of adults dying with COPD, Chest 122 (2002) 2003–2008.

[18] M. Miravitlles, M. Ferrer, A. Pont, et al., Characteristics of a population of COPD patients identified from a population based study. Focus on previous diagnosis and never smokers, Respir. Med. 99 (8) (2005) 985–995.
[19] X. Xu, S.T. Weiss, B. Rijcken, J.P. Schouten, Smoking, changes in smoking habits, and rate of decline in FEV1: new insight into gender differences, Eur. Respir. J. 7 (6) (1994) 1056–1061.
[20] E.K. Silverman, S.T. Weiss, J.M. Drazen, et al., Gender-related differences in severe, early-onset chronic obstructive pulmonary disease, Am. J. Respir. Crit. Care Med. 162 (6) (2000) 2152–2158.
[21] M.T. Dransfield, J.J. Davis, L.B. Gerald, W.C. Bailey, Racial and gender differences in susceptibility to tobacco smoke among patients with chronic obstructive pulmonary disease, Respir. Med. 100 (6) (2006) 1110–1116.
[22] E. Melbostad, W. Eduard, P. Magnus, Chronic bronchitis in farmers, Scand. J. Work Environ. Health 23 (1997) 271–280.
[23] E. Zuskin, J. Mustajbegovic, E.N. Schachter, J. Doko-Jelinic, Respiratory function of textile workers employed in dyeing cotton and wool fibers, Am. J. Ind. Med. 31 (1997) 344–352.
[24] A.D. Oxman, D.C. Muir, H.S. Shannon, et al., Occupational dust exposure and chronic obstructive pulmonary disease. A systematic overview of the evidence, Am. Rev. Respir. Dis. 148 (1993) 38–48.
[25] P.S. Bakke, V. Baste, R. Hanoa, A. Gulsvik, Prevalence of obstructive lung disease in a general population: relation to occupational title and exposure to some airborne agents, Thorax 46 (1991) 863–870.
[26] R.J. Korn, D.W. Dockery, F.E. Speizer, et al., Occupational exposures and chronic respiratory symptoms. A population-based study, Am. Rev. Respir. Dis. 136 (1987) 298–304.
[27] J. Balmes, M. Becklake, P. Blanc, et al., Environmental and Occupational Health Assembly, American Thoracic Society. American Thoracic Society Statement: Occupational contribution to the burden of airway disease, Am. J. Respir. Crit. Care Med. 167 (5) (2003) 787–797.
[28] P.D. Blanc, K. Toren, Occupation in chronic obstructive pulmonary disease and chronic bronchitis: an update, Int. J. Tuberc. Lung Dis. 11 (2007) 251–257.
[29] E. Hnizdo, P.A. Sullivan, K.M. Bang, G. Wagner, Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study of data from the Third National Health and Nutrition Examination Survey, Am. J. Epidemiol. 156 (2002) 738–746.
[30] S. Weinmann, W.M. Vollmer, V. Breen, et al., COPD and occupational exposures: a case-control study, J. Occup. Environ. Med. 50 (2008) 561–569.
[31] L. Trupin, G. Earnest, M. San Pedro, et al., The occupational burden of chronic obstructive pulmonary disease, Eur. Respir. J. 22 (2003) 462–469.
[32] A.D. Lopez, C.D. Mathers, M. Ezatti, et al., Global Burden of Disease and Risk Factors, World Bank, Washington, DC, 2006.
[33] Sundeep S. Salvi, Peter J. Barnes, Chronic obstructive pulmonary disease in non-smokers, Lancet 374 (2009) 733–743.
[34] K.R. Smith, Inaugural article: national burden of disease in India from indoor air pollution, Proc. Natl. Acad. Sci. USA 97 (24) (2000) 13286–13293.
[35] M. Chan-Yeung, N. Aït-Khaled, N. White, M.S. Ip, W.C. Tan, The burden and impact of COPD in Asia and Africa, Int. J. Tuberc. Lung Dis. 8 (1) (2004) 2–14.
[36] M. Ezzati, Indoor air pollution and health in developing countries, Lancet 366 (9480) (2005) 104–106.
[37] M. Oroczo-Levi, J. Garcia-Aymerich, J. Villar, et al., Wood smoke exposure and risk of chronic obstructive pulmonary disease, Eur. Respir. J. 27 (3) (2006) 542–546.
[38] A. Ekici, M. Ekici, E. Kurtipek, et al., Obstructive airway diseases in women exposed to biomass smoke, Environ. Res. 99 (1) (2005) 93–98.
[39] A. Ramírez-Venegas, R.H. Sansores, R. Pérez-Padilla, et al., Survival of patients with chronic obstructive pulmonary disease due to biomass smoke and tobacco, Am. J. Respir. Crit. Care Med. 173 (4) (2006) 393–397.
[40] E. Nizankowska-Mogilnicka, F. Mejza, A.S. Buist, et al., Prevalence of COPD and tobacco smoking in Malopolska region—results from the BOLD study in Poland, Pol. Arch. Med. Wewn. 117 (9) (2007) 402–410.
[41] P. Yin, C.Q. Jiang, K.K. Cheng, et al., Passive smoking exposure and risk of COPD among adults in China: the Guangzhou Biobank Cohort Study, Lancet 370 (9589) (2007) 751–757.
[42] M.D. Eisner, J. Balmes, P.P. Katz, et al., Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease, Environ. Health 4 (1) (2005) 7–14.
[43] M. Simoni, S. Baldacci, R. Puntoni, et al., Respiratory symptoms/diseases and environmental tobacco smoke (ETS) in never smoker Italian women, Respir. Med. 101 (3) (2007) 531–538.
[44] C. Iribarren, G.D. Friedman, A.L. Klatsky, M.D. Eisner, Exposure to environmental tobacco smoke: association with personal characteristics and self reported health conditions, J. Epidemiol. Community Health 55 (10) (2001) 721–728.
[45] M.L. Larsson, H.M. Loit, M. Meren, et al., Passive smoking and respiratory symptoms in the FinEsS Study, Eur. Respir. J. 21 (4) (2003) 672–676.
[46] B.R. Celli, C.G. Cote, J.M. Marin, et al., The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease, N. Engl. J. Med. 350 (2004) 1005–1012.
[47] S. Chinn, D. Jarvis, P. Burney, Relation of bronchial responsiveness to body mass index in the ECRHS, Thorax 57 (2002) 1028–1033.
[48] D.J. Berglund, D.E. Abbey, M.D. Lebowitz, et al., Respiratory symptoms and pulmonary function in an elderly nonsmoking population, Chest 115 (1999) 49–59.
[49] G.E. Silva, D.L. Sherrill, S. Guerra, R.A. Barbee, Asthma as a risk factor for COPD in a longitudinal study, Chest 126 (2004) 59–65.
[50] C.S. Ulrik, P. Lange, Decline of lung function in adults with bronchial asthma, Am. J. Respir. Crit. Care Med. 150 (1994) 629–634.
[51] A. Abhyankar, S. Salvi, Prevalence of COPD with reversible obstruction in first spirometries, among patients with obstructive airways disease in western Maharashtra, India, in: European Respiratory Society Annual Conference, Berlin, Germany; October 4–8, 2008. Abstr. E456.