Prevalence and predictors of chronic obstructive pulmonary disease among high-risk Egyptians

Azza F. Said[a], Ashraf A. Ewis[b], Ahmad A. Omran[c], Mohamed E. Magdy[a], Micheal F. Saleeb[d]

Background Chronic obstructive pulmonary disease (COPD) is the fourth most common cause of death in the world. COPD prevalence, morbidity, and mortality vary across countries and across different groups within countries. In Egypt, COPD is a rising significant health problem; however, information on its prevalence, morbidity, and mortality is still lacking.

Aim of the study The first aim was to detect the prevalence of COPD among high-risk Egyptians Global using Initiative for Chronic Obstructive Lung Disease (GOLD) and FEV_1/FVC < lower limit of normal (LLN) definitions. The second goal was to identify the factors predictive for diagnosis of COPD.

Patients and methods This study included 363 randomly selected individuals with a high risk for COPD; 176 were smokers (group I), 107 were construction and brick manufacturer workers (group II), and 80 were women exposed to biomass fuel (group III). All individuals filled out a respiratory questionnaire, were clinically examined, and subjected to spirometric evaluation.

Results The prevalence of COPD among high-risk individuals was 9.6 and 17.4% on the basis of GOLD and LLN, respectively. The sensitivity and specificity of prebronchodilator values of FEV_1/FVC < LLN were 94.3 and 90.8%, respectively, for the diagnosis of COPD. However, our findings support that the postbronchodilator LLN definition is superior in ruling out the presence of COPD, as it has a good negative test specificity of 99.7%. Chest wheezes were the only symptom that was an independent predictor of COPD (odds ratio 4.80, 95% confidence interval 1.57–14.74, $P = 0.02$). Increasing age, smoking, and mean pack-years were also factors predictive for COPD.

Conclusion The prevalence of COPD among high-risk individuals in Egypt was estimated to be about 10% as per GOLD. Prebronchodilator LLN is a reliable method for the diagnosis of COPD and it yields comparable results to the GOLD criteria. The main predictors for COPD diagnosis are old age, smoking history, and presence of chest wheezes.
Egypt J Broncho 2015 9:27–33

Egyptian Journal of Bronchology 2015 9:27–33

Keywords: chronic obstructive pulmonary disease, Global Initiative for Chronic Obstructive Lung Disease, high-risk groups, lower limit of normal

Departments of [a]Chest Diseases [b]Public Health and Occupational Medicine [c]Clinical Pathology, Faculty of Medicine, Minia University [d]Mallawy Chest Hospital, Ministry of Health, Minia City, Egypt

Correspondence to Azza Farag Said, MD, Department of Chest Diseases, Faculty of Medicine, Minia University, Minia, 61111, Egypt
Tel: 0862355846;
E-mail: azza20022@yahoo.com

Received 12 October 2014 **Accepted** 02 November 2014

Introduction

Chronic obstructive pulmonary disease (COPD) prevalence, morbidity, and mortality vary across countries and across different groups within countries with a direct relation to the prevalence of tobacco smoking. Other risk factors for COPD include genetic factors, longstanding asthma, outdoor air pollution, second-hand smoke exposure, biomass smoke, indoor air pollution, occupational exposures, and tuberculosis [1]. The prevalence and burden of COPD are projected to increase in the coming decades because of continued exposure to COPD risk factors and the changing age structure of the world's population. As these factors are rapidly increasing in developing countries, COPD will become a major health problem, exerting a huge demand on economic and healthcare resources in developing countries [2].

In Egypt, although COPD is a rising significant health problem, data on its prevalence, morbidity, and mortality are still lacking and have to be estimated [3]. Because currently available treatments have minimal impact on disease progression, a strategy for early diagnosis of COPD is a critical priority. Early implementation of spirometry for individuals at risk may identify the disease in its early stages [1].

In 2001, the Global Initiative for Chronic Obstructive Lung Disease committee was the first to publish a consensus statement propagating the use of a fixed FEV_1/FVC < 0.70 value and fixed FEV_1 values to classify severity [4]. The choice of a fixed cutoff point for the GOLD-COPD definition was made for generalization and simplification [5]. However, more recently the GOLD committee recognized that using a fixed value of less than 0.70 may lead to potential overdiagnosis of COPD in the elderly as the FEV_1 value decreases more quickly with age than the FVC [6]. The American Thoracic Society (ATS) and the European Respiratory Society (ERS) proposed using a threshold below the lower limit of normal adjusted for age instead of a fixed criterion

for FEV_1/FVC [7]. They defined the LLN as the fifth percentile of reference values drawn from the Third National Health and Nutrition Examination Survey (NHANES-III) cohort [8]. Calculation of LLN is based on multiple regression calculations and may be subject to considerable variability around the median and is affected by sex and race [9], and a value of FEV_1/FVC below the LLN of an age-matched healthy reference group is considered abnormal and consistent with a diagnosis of COPD [10,11].

Aim of the work

The first objective of this study was to identify the prevalence of COPD among high-risk individuals using GOLD and FEV_1/FVC < LLN definitions, with estimation of the accuracy of using the FEV_1/FVC < LLN for diagnosis of COPD. The second aim was to detect predicting factors for COPD diagnosis.

Patients and methods

A total of 363 randomly selected individuals at high risk for COPD were studied from January 2011 to September 2013. This study was approved by the ethical committee of the Faculty of Medicine, Minia University. Informed consent was obtained from all participants. They were divided into three groups:

Group I: This group included 176 individuals aged 40 years or older with a smoking history of at least 10 pack-year (current or ex-smoker). They were relatives or visitors of patients admitted to Mallawy Chest Hospital, Minia Government, Egypt.

Group II: This group involved 107 workers who were engaged in construction and/or brick manufacturing.

Group III: This group comprised 80 randomly selected women with a history of exposure to biomass fuel in a poorly ventilated dwelling from two villages (Tahna El-Gabal and El-Arean) of Minia City.

Individuals with a history of known chronic cardiorespiratory diseases and those with collagen vascular diseases were excluded.

All participants were subjected to the following:

(1) A questionnaire including age, sex, smoking status, presence of chronic cough, chronic sputum production, chest wheezing, and shortness of breath; grading of dyspnea using a modified medical research council (MMRC) dyspnea scale.
(2) General examination, including measurements of body weight, height, and BMI.
(3) Local chest examination.
(4) Spirometry was performed on those with one or more positive symptoms in the respiratory questionnaire using a calibrated digital hand-held spirometer (TED, SPANSH). The best of three measurements was obtained while the patients were in the seated position. Values were obtained while the participant exerted his or her maximum effort were used so as to avoid any expected error in diagnosis. Results were obtained for FVC, FEV_1, ratio of FEV_1/FVC (FEV_1/FVC%), forced expiratory flow at 25–75% of vital capacity, and peak expiratory flow. The absolute values and the percentages of spirometric parameters predicted from the participant's age, sex, and height were calculated. Individuals who had FEV1/FVC < 70% and FEV1 < 80% predicted with FVC ≥ 80% were asked to perform a postbronchodilator spirometry test 20 min after two puffs of 200 μg salbutamol.

A postbronchodilator FEV_1/FVC < 70% of predicted established the diagnosis of 'GOLD-COPD' [4]. Values of FEV_1/FVC < LLN in an age-matched healthy reference group were considered abnormal and consistent with a diagnosis of 'LLN-COPD' [10,11].

From several LLN equations provided we selected LLN prediction equations as per the study by Hankinson *et al*. [8]. LLN equations for FEV_1/FVC% specific for sex, ethnicity, and age were derived from the NHANES-III database for ages 8–80 years.

LLN of FEV_1/FVC for males = 78.38–0.206 × age,

LLN of FEV_1/FVC of females = 81.01–0.212 × age.

Free software with documentation for all ethnic groups is now available and was also used in this study [12].

COPD patients who were diagnosed under both definitions were further examined by means of a chest radiograph, complete blood count, C-reactive protein (CRP) levels, and sputum culture on chocolate agar media.

Statistical analysis

Statistical analyses were performed using the statistical package for social sciences (SPSS) program, version 16. Differences in the mean of quantitative variables were analyzed using parametric tests (the independent sample *t*-test, one-way analysis of variance test), and differences between categorical variables were analyzed using the χ^2-test. For all tests, the values of *P*-value less than 0.05 were regarded as statistically significant.

Results

A total of 363 individuals with high risk for COPD participated in the study and they were divided into

three groups. Group I (176, 48.5%) comprised smokers of male sex and their mean age was 51.2 years with a smoking history of at least 10 pack-years. Group II included 107 (29.5%) individuals; 55 (51.8%) were construction workers and 52 (48.2%) were brick manufacturers and 91.6% of them were current smokers. Group III comprised 80 (22%) women with a positive history for biomass exposure. They were exposed to high levels of indoor air pollution due to biomass cooking or heating in their houses for at least 20 years (Table 1).

Tables 2, 3, and 4 show the prevalence of COPD on the basis of GOLD and prebronchodilator and postbronchodilator FEV_1/FVC < LLN criteria as 9.6, 17.4, and 8.9%, respectively. The prevalence of COPD was not significantly different among the studied groups on either GOLD or LLN criteria (P = 0.7, 0.2, and 0.58, respectively).

On determining the accuracy of FEV_1/FVC < LLN for the diagnosis of COPD, we considered GOLD as the gold standard 'Reference test' for diagnosis of COPD and compared FEV_1/FVC < LLN with it. First, we compared prebronchodilator FEV_1/FVC < LLN with that of GOLD and found that 33 of 35 participants had COPD on the basis of both criteria, giving a sensitivity of 94.3%. Second, on using the postbronchodilator value of FEV_1/FVC < LLN, it was found that 31 of 35 participants had COPD on the basis of both criteria, resulting in a sensitivity of 88.6%. On assessment of specificity of prebronchodilator FEV_1/FVC < LLN, it was found that 298 out of 328 did not have COPD on the basis of either criteria, yielding a specificity of 90.8%. However, for postbronchodilator FEV_1/FVC < LLN, it increased to 99.7% (327 out of 328 participants had no COPD on the basis of either criteria) (Table 5).

The GOLD-COPD was graded using postbronchodilator % of predicted FEV_1 values: GOLD 1 (mild), $FEV_1 \geq 80\%$; GOLD 2 (moderate), FEV_1 < 80% predicted but ≥ 50% predicted; GOLD 3 (severe), FEV_1 < 50% predicted but ≥30% predicted; and GOLD 4 (very severe), FEV_1 < 30% predicted [10]. According to the severity criteria of GOLD, the prevalence of GOLD 1 (mild), GOLD 2 (moderate), GOLD 3 (severe), and GOLD 4 (very severe) COPD was 3, 69, 17, and 11%, respectively (Fig. 1). Moderate grade (GOLD 2) was the most frequently seen (24 out of 35 patients, 69%) with closely related distribution among the three studied groups (nine patients in group I, eight in group II, and seven in group III). In

Table 1 Descriptive data of all participants

Variables	Group I (*n* = 176)	Group II (*n* = 107)	Group III (*n* = 80)
Age			
Range	40–74	24–67	36–61
Mean ± SD	51.2 ± 7	49.4 ± 7.8	45.9 ± 5.3
Sex			
Male	176 (62.2)	107 (37.8)	0 (0)
Female	0 (0)	0 (0)	80 (100)
Smoking status			
Current smoker	166 (94.4)	98 (91.6)	4 (5)
Ex-smoker	10 (5.6)	3 (2.8)	7 (8.8)
Nonsmoker	0 (0.6)	6 (5.6)	69 (86.2)
BMI			
<18.5	0 (0)	0 (0)	1 (100)
18.5–24.9	138 (47.9)	96 (33.3)	54 (18.8)
25–29.9	37 (52.1)	11 (15.5)	23 (32.4)
≥30	1 (33.3)	0 (0)	2 (66.7)
Range	19.4–30.4	19.8–29.4	16.6–30.4
Mean ± SD	23.6 ± 1.7	23.3 ± 1.6	24.1 ± 2.4

Data are represented as *n* [%], whereas for age and BMI, it is presented as range and mean ± SD.

Table 2 Prevalence of COPD among the studied groups as defined by GOLD criteria

Variables	Group I (*n* = 176)	Group II (*n* = 107)	Group III (*n* = 80)	Total	*P*-value
COPD	15 (8.5)	11 (10.3)	9 (11.2)	35 (9.6)	0.7
Non-COPD	161 (91.5)	96 (89.7)	71 (88.8)	328 (90.4)	

Data are represented as *n* [%]; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 3 Prevalence of COPD among the studied groups by prebronchodilator FEV_1/FVC < LLN

Variables	Group I (*n* = 176)	Group II (*n* = 107)	Group III (*n* = 80)	Total	*P*-value
COPD	28 (15.9)	16 (15)	19 (23.8)	63 (17.4)	0.2
Non-COPD	148 (84.1)	91 (85)	61 (76.2)	300 (82.6)	

Data are represented as *n* [%]; COPD, chronic obstructive pulmonary disease; LLN, lower limit of normal.

Table 4 Prevalence of COPD among the studied groups by postbronchodilator FEV_1/FVC < LLN

Variables	Group I (*n* = 176) [*n* (%)]	Group II (*n* = 107) [*n* (%)]	Group III (*n* = 80) [*n* (%)]	Total [*n* (%)]	*P*-value
COPD	13 (7.4)	10 (9.4)	9 (11.2)	32 (8.9)	0.58
Non-COPD	163 (92.6)	97 (90.6)	71 (88.8)	331 (91.1)	

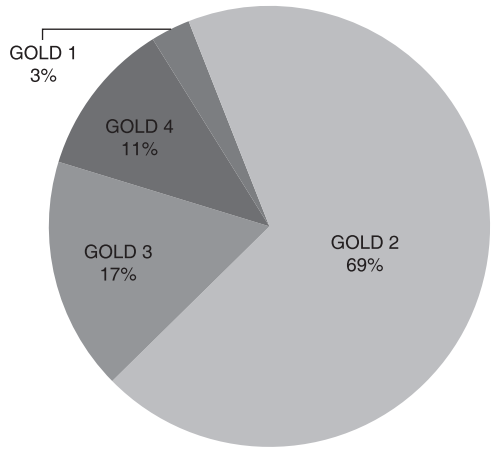
COPD, chronic obstructive pulmonary disease; LLN, lower limit of normal.

Table 5 Diagnostic accuracy of FEV_1/FVC < LLN

Variables	Sensitivity (%)	Specificity (%)	Positive predicted value (%)	Negative predicted value (%)	Accuracy (%)	Error %
Prebronchodilator FEV_1/FVC < LLN	94.3	90.8	52.4	99.3	91.2	8.8
Postbronchodilator FEV_1/FVC < LLN	88.6	99.7	96.9	98.8	98.6	1.4

LLN, lower limit of normal.

Fig. 1



Global Initiative for Chronic Obstructive Lung Disease (GOLD) grading among 35 chronic obstructive pulmonary disease patients.

contrast, all four (11%) patients with COPD grade 4 (very severe) were from group I.

Discussion

This study was designed to detect the prevalence of COPD among high-risk individuals on the basis of GOLD and LLN definitions. Using the GOLD definition, the prevalence of COPD was found to be 9.6% (Table 2). Estimates of prevalence from industrialized countries range widely, reflecting both true differences as well as differences in the definition of COPD and the diagnostic tools used in the surveys, and whether spirometry was used to confirm the diagnosis. Most studies find a prevalence of 10–15% in the population above 35–40 years of age [13–17]. An international survey (BREATH Study) [18] in a large sample of individuals aged 40 years and above in 12 countries of the MENA region showed that 3.6% of individuals fulfilled the epidemiological definition of COPD.

Most studies estimated the prevalence of COPD in general population samples and not among those at high risk only. Hill *et al.* [19] detected the prevalence of COPD among patients at risk in primary care (age ≥40 years with a smoking history of 20 pack-years) to be 20.7%. Another study by Zielinski and Bednarek [20] found that spirometric signs of airway obstruction were found in 24.3% of individuals at high risk for COPD (smokers who were >39 years old with a smoking history of >10 pack-years).

The prevalence of COPD was higher in this study when the prebronchodilator FEV_1/FVC < LLN definition was used (Table 3) compared with the GOLD definition (17.4 vs. 9.6%, respectively) and closer to that of GOLD on using postbronchodilator FEV_1/FVC < LLN (8.9%) (Table 4). This could be attributed to the fact that the LLN definition could diagnose obstructive airway diseases other than COPD, such as asthma, as in 28 of 63 patients on LLN definition the postbronchodilator values of FEV_1/FVC were more than 70% predicted.

This study revealed that both occupational exposure and biomass fuel use contribute to the presence of COPD as a risk factor to a similar extent as smoking ($P > 0.05$).

There is an evidence-based review that presents an overview of studies comparing the FEV_1/FVC < LLN with FEV_1/FVC < 0.70 in diagnosing spirometry-based COPD [21]. The majority of studies concluded that using the FEV_1/FVC < 0.70 approach resulted in a greater prevalence of COPD, which was often interpreted as 'overdiagnosing COPD'. All these studies were performed in western countries and almost uniformly did not include postbronchodilator values as recommended by GOLD-COPD.

In accordance with our results, Aggarwal *et al.* [22] found an overall lower prevalence rate when applying FEV_1/FVC < 0.70 instead of the LLN (23.6 and 28.2%, respectively). This study was performed in India and was composed of 56.1% men of a mean age of 48.2 years. Another study in Lebanon [23] found that the prevalence of COPD as per GOLD was 9.7% [95% confidence interval (CI) 8.5–10.9%] and as per LLN was 12.5% (95% CI 11.2–13.9%).

However, all previous studies on LLN and GOLD compared the two methods without application of a reference test. Without a reference, however, it is impossible to determine which method performs better [24].

Although the LLN might be a statistically more sound method of diagnosing airflow obstruction compared with the fixed ratio, it has not been clinically validated for want of a gold standard. Longitudinal studies of outcomes comparing the two methods of defining cutoffs have been equivocal [25].

On determining the accuracy of FEV_1/FVC < LLN for the diagnosis of COPD, we found that the sensitivity of prebronchodilator FEV_1/FVC < LLN was higher than the postbronchodilator value (94.3 and 88.6%, respectively). The positive and negative predicted values and accuracy of prebronchodilator FEV_1/FVC < LLN were 52.9, 99.3, and 91.2%, respectively, whereas that of postbronchodilator values were 96.9, 98.8, and 98.6%, respectively. In contrast, specificity of postbronchodilator FEV_1/FVC < LLN was nearly 100% (99.7%) (Table 5).

Kato *et al.* [26] found that FEV_1/FVC < LLN had a sensitivity of 65.0% and specificity of 100% for the diagnosis of COPD. Güder *et al.* [27] used the consensus of an expert panel as a reference standard for COPD, which is accepted as the best alternative in the absence of a true reference standard. They found that the sensitivity and specificity of GOLD for the diagnosis of COPD as compared with the reference test were 85.4 and 79.1%, respectively. They also found the sensitivity and specificity of FEV_1/FVC < LLN to be 55.1 and 96.2%.

COPD is and remains a clinical diagnosis, and therefore a panel decision on its absence or presence by taking into account all relevant clinical factors, such as age, respiratory complaints, smoking history, etc. is the classical approach. The fixed FEV_1/FVC <0.70 criterion and the LLN should subsequently be compared with the panel diagnosis of COPD and the sensitivity/specificity evaluated [21].

Regarding the classification of the severity of COPD by GOLD using postbronchodilator values of FEV_1, we found that grade II (moderate) and grade III (severe) were higher than the other grades of COPD (68.6 and 17.1%, respectively) (Fig. 1). The prevalence of early COPD is high and varies significantly between countries. In the BOLD study, the prevalence of GOLD stage I COPD ranged from 1% in the Philippines to 16% in Austria, whereas that of GOLD stage II COPD ranged from 5% in Germany to 12% in South Africa [13]. Distribution of COPD stage in COPD patients in Lebanon was as follows: 17.6% mild (stage I), 58.3% moderate (stage II), 20.3% severe (stage III), and 3.8% very severe (stage IV) [23]. Another study in Copenhagen revealed that 6.2% of patients had mild COPD, 9.2% had moderate COPD, and 2.0% had severe or very severe COPD [28]. Deveci *et al*. [29] performed a study in Turkey and found that the majority of COPD cases were at stages I and II (22.6 and 66%, respectively). Unfortunately, in the current study, grade I (mild COPD) had the lowest frequency (2.9%) and all cases of grade 4 were found among group I participants only.

It is clear from our study and from other studies conducted in the Middle East that moderate grade of COPD is more frequent than other grades.

On considering the predicting factors for COPD using GOLD criteria, it was found that age 50 years, 12.5 pack-years, and chest wheezes were the highest independent factors for the presence of COPD (Table 6). As per the LLN criteria, we found that current smokers, ex-smokers, 12.5 pack-years, and chest wheezes were also high-risk factors (Table 7). Minas *et al.* [30] found that male sex (P = 0.001), older age (P < 0.001), a smoking habit of more than 10 pack-years (P < 0.001), and the presence of respiratory symptoms, mainly cough, sputum production, dyspnea, and wheezing (P < 0.001), were the most significant factors related to the presence of COPD. Sandelowsky

Table 6 Regression analysis for prediction of COPD by GOLD definition

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age (~50 years)	2.42 (1.16–5.03)	0.02	1.74 (0.99–4.12)	0.033
Female sex	1.25 (0.65–2.79)	0.7	1.07 (0.66–2.56)	0.5
Occupation	1.23 (0.54–2.97)	0.4	1.16 (1.02–2.19)	0.3
Biomass fuel	1.36 (0.57–3.25)	0.6	1.31 (1.01–3.45)	0.9
Smokers+ex-smokers	0.91 (0.87–0.94)	0.1	0.86 (1.03–9.34)	0.11
Pack-year (12.5)	2.38 (0.99–5.72)	0.047	1.78 (0.76–4.03)	0.01
Chest wheezes	4.80 (1.57–14.74)	0.021	2.57 (1.38–4.63)	0.01
Expectoration	0.72 (0.20–2.58)	0.9	0.48 (0.23–0.77)	0.28

CI, confidence interval; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio.

Table 7 Regression analysis for prediction of COPD by FEV_1/FVC < LLN

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age (~50 years)	1.34 (0.78–2.32)	0.16	1.14 (0.88–3.37)	0.9
Female sex	1.69 (0.92–3.11)	0.8	1.39 (0.96–3.28)	0.23
Occupation	0.93 (0.48–1.81)	0.11	1.02 (0.78–2.22)	0.34
Biomass fuel	1.65 (0.86–3.17)	0.12	1.35 (1.06–4.66)	0.3
Smokers+ex-smokers	1.68 (0.21–13.62)	0.048	1.86 (1.01–8.11)	0.023
Pack-year (12.5)	2.09 (1.06–4.13)	0.03	2.17 (0.93–3.64)	0.012
Chest wheezes	2.26 (0.76–6.76)	0.002	2.02 (0.87–5.66)	0.01
Expectoration	0.43 (0.17–1.10)	0.4	0.33 (0.14–0.87)	0.7

CI, confidence interval; COPD, chronic obstructive pulmonary disease; LLN, lower limit of normal; OR, odds ratio.

et al. [31] revealed a statistically significant association between COPD and age of 55 years and above (odds ratio 10.9, 95% CI 3.8–30.1, $P < 0.001$) and between COPD and pack-years of 20 or more (odds ratio 3.2, 95% CI 1.2–8.5, $P = 0.016$) in current smokers as positive predictors for COPD.

The chronic inflammation in COPD, orchestrated by multiple inflammatory cells and mediators in the airways and lung tissues, is induced by inhalation of noxious gases and particulate matter. This persistent inflammatory response in the lung is also associated with a significant systemic inflammatory response yielding adverse clinical outcomes, the so-called systemic effects of COPD. Although the origin of systemic inflammation present in COPD remains poorly understood, it is clearly established that some inflammatory markers are raised in systemic circulation. Of the blood-based biomarkers, CRP has shown the greatest promise [32].

In patients with COPD, increased CRP levels are associated with poor lung function, reduced exercise capacity, and worse quality of life. It is also a significant predictor of all-cause mortality [33]. CRP increase in COPD patients may be either due to the disease itself causing systemic inflammation or due to related factors such as ischemic heart disease and cigarette smoking [34].

In the present study we assessed CRP among patients with COPD and it was found that the number of patients with positive CRP was significantly higher than the number of patients with negative CRP (57.1 vs. 42.9%, respectively, $P = 0.009$) on the basis of the GOLD definition (Table 8).

The lower airways have until recently been considered a sterile environment, and in airway diseases such as bronchiectasis and COPD the isolation of bacteria such as *Hemophilus influenzae* and pseudomonas species in sputum samples by culture is not uncommon. Although these pathogens are often associated with exacerbations, they are also often present during stable phase of the airways disease, indicating chronic colonization [35,36].

Sputum microbiology was assessed in this work among COPD patients and we found that COPD patients by GOLD definition had a significantly higher proportion of Gram-negative organisms in sputum culture compared with other microorganisms (Table 9). In accordance with this result, Bari *et al.* [37] found that the prevalence of lower airway bacterial colonization in outpatients with stable COPD is high and is mainly due to Gram-negative bacilli like Pseudomonas.

Table 8 CRP among COPD patients

Variables	CRP+	CRP–	*Z*	*P*-value
GOLD-COPD (*n* = 35)	20 (57.1)	15 (42.9)	2.36	0.009
LLN-COPD (*n* = 63)	35 (55.6)	28 (44.4)	0.85	0.196

Data are represented as *n* [%]; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LLN, lower limit of normal; $P < 0.05$, significant.

Table 9 Sputum culture results among COPD patients

Variables	Gram-positive	Gram-negative	Mixed organism	*Z*	*P*-value
GOLD-COPD (*n* = 35)	11 (31.4)	17 (48.6)	7 (20)	1.89	0.029
LLN-COPD (*n* = 63)	24 (38)	21 (33.5)	18 (28.5)	1.16	0.124

Data are represented as *n* [%]; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LLN, lower limit of normal; $P < 0.05$, significant.

Certain limitations need to be considered in the interpretation of our findings. First, our work was carried out only on high-risk individuals and not on general population samples. Second, we used reference equations for $FEV_1/FVC <$ LLN from the USA that may not ideally apply to our population. This may result in biased outcomes because of nonavailability of population-specific reference equations in our locality. Although a free software is now available for different races, its accuracy with respect to the reference equations has not been established. The other limiting factor was the small sample of individuals assessed.

The main strength of the present study is the inclusion of risk factors other than smoking in the evaluation of COPD prevalence, as well as the use of postbronchodilator values of FEV_1/FVC in the LLN definition.

Conclusion

This study showed that the prevalence of COPD among high-risk Egyptians by GOLD and LLN criteria was 9.6 and 17.4%, respectively. The present study showed a higher prevalence of grade 2 (69%) and grade 3 (17%) and lower prevalence of grade 1 (3%) COPD. Prebronchodilator $FEV_1/FVC <$ LLN had a high sensitivity and specificity for COPD diagnosis. The postbronchodilator LLN definition is superior in ruling out the presence of COPD as a good negative test.

Age 50 years, pack-years of 12 or more, and chest wheezing were strong predictors of COPD; therefore, spirometry in high-risk groups, especially if they had these predictors, can help detect COPD in early stages.

Increasing awareness of COPD in the general population and specifically among high-risk individuals can aid in the early diagnosis of this disease.

Our results highlight COPD as a major public health problem in Egypt and call for more research to be directed toward preventive measures and efforts.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Eisner MD, Anthonisen N, Coultas D, Kuenzl N, Perez-Padilla R, Postma D, *et al.* An Official American Thoracic Society Public Policy Statement: novel risk factors and the global burden of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2010; **182**:693–718.

2 Chan-Yeung M, Ait N, White N, IP M, Tan WC. The burden and impact of COPD in Asia and Africa. *Int J Tuberc Lung* 2004; **8**:2–14.

3 Egyptian Society of Chest Diseases and Tuberculosis (ESCT). The Egyptian guidelines for the management of chronic obstructive pulmonary disease. *Egypt J Chest Dis Tub* 2003; **52**:1–28.

4 Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001; **163**:1256–1276.

5 Calverley PM. The GOLD classification has advanced understanding of COPD. *Am J Respir Crit Care Med* 2004; **170**:211–212.

6 Rabie 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**:532–555.

7 Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al.* Standardization of spirometry. *Eur Respir J* 2005; **26**:319–338.

8 Hankinson JL, Odencrantz JR, Fedan KB. Spiro metric reference values from a sample of the general US population. *Am Rev Respir Crit Care Med* 1999; **159**:179–187.

9 Stanojevic S, Wade A, Stocks J, Hankinson J, Coates AL, Pan H, *et al.* Reference ranges for spirometry across all ages: a new approach. *Am J Respir Crit Care Med* 2008; **177**:253–260.

10 Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, *et al.* Interpretative strategies for lung function tests. *Eur Respir J* 2005; **26**:948–968.

11 Swanney MP, Ruppel G, Enright PL, Pedersen OF, Crapo RO, Miller MR, *et al.* Using the lower limit of normal for the FEV_1/FVC ratio reduces the misclassification of airway obstruction. *Thorax* 2008; **63**:1046–1051.

12 Quanjer PH Available at: *http://www.spirxpert.com/GOLD.html*. [Last accessed on 2008 Dec 1]

13 Buist AS, Mcburnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, *et al.* International variation in the prevalence of COPD (The BOLD Study): a population- based prevalence study. *Lancet* 2007; **370**:741–750.

14 Lindberg A, Jonsson AC, Ro¨nmark E, Lundgren R, Larsson LG, Lundba¨ck B. Prevalence of chronic obstructive pulmonary disease according to BTS, ERS, GOLD and ATS criteria in relation to doctor's diagnosis, symptoms, age, gender and smoking habits. *Respiration* 2005; **72**:471–479.

15 Menezes AMB, Perez-Padilla R, Jardim JRB, Mujoo A, Lopez MV, Valdivia G, *et al.* Chronic obstructive pulmonary disease in five Latin American cities (the Platino study): a prevalence study. *Lancet* 2005; **366**:1875–1881.

16 Lindberg A, Bjerg-Backlund A, Ro¨nmark E, Larsson LG,Lundba¨ck B. Prevalence and under diagnosis of COPD by disease severity and the attributable fraction of smoking: report from the obstructive lung disease in Northern Sweden studies. *Respir Med* 2006; **100**:264–272.

17 Kim DS, Kim YS, Jung KS, Chang JH, Lim CM, Lee JH, *et al.* Prevalence of chronic obstructive pulmonary disease in Korea: a population-based spirometry survey. *Am J Respir Crit Care Med* 2005; **172**:842–847.

18 Tageldin MA, Nafti S, Khan JA, Nejjari C,Beji M, Mahboub B, *et al.* Distribution of COPD-related symptoms in the Middle East and North Africa: results of the BREATHE study. *Respir Med* 2012; **106**:S25–S32.

19 Hill K, Goldstein RS, Guyatt GH, Blouin M,Tan WC, Davis LL, *et al.* Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. *CMAJ* 2010; **182**:673–678.

20 Zielinski J, Bednarek M. Early detection of COPD in a high-risk population using spirometric screening. *Chest* 2001; **119**:731–736.

21 Hoesein FAM, Zanen P, Lammers JW. Lower limit of normal or FEV1/FVC < 0.70 in diagnosing COPD: an evidence-based review. *Respir Med* 2011; **105**:907–915.

22. Aggarwal AN, Gupta D, Behera D, Jindal SK. Comparison of fixed percentage method and lower confidence limits for defining limits of normality for interpretation of spirometry. *Respir Care* 2006; **51**:737–743.

23 Waked M,Khayat G, Salameh P. Chronic obstructive pulmonary disease prevalence in Lebanon: a cross-sectional descriptive study.*Clin Epidemiol* 2011; **3**:315–323.

24 Moons KG, Grobbee DE. When should we remain blind and when should our eyes remain open in diagnostic studies? *J Clin Epidemiol* 2002; **55**:633–636.

25 Vaz Fragoso CA, Concato J, McAvay G, Van Ness PH, Rochester CL, Yaggi HK, Gill TM. Chronic obstructive pulmonary disease in older persons: a comparison of two spirometric definitions. *Respir Med* 2010; **104**:1189–1196.

26 Kato B, Gulsvik A, Vollmer W, Janson C, Studnika M, Buist S, Burney P. Can spirometric norms be set using pre- or post-bronchodilator test results in older people? *Respir Res* 2012; **13**:102.

27 Güder G, Brenner S, Angermann CE, Ertl G, Held M, Sachs AP *et al.* GOLD or lower limit of normal definition? A comparison with expert-based diagnosis of chronic obstructive pulmonary disease in a prospective cohort-study. *Respir Res* 2012; **13**:13.

28 Fabricius P, Løkke A, Marott JL, Vestbo J, Lange P. Prevalence of COPD in Copenhagen. *Respir Med* 2011; **105**:410–417.

29 Deveci F, Deveci SE, Türkoğlu S, Turgut T, Kirkil G Rahman S, *et al.* The prevalence of chronic obstructive pulmonary disease in Elazig, Eastern Turkey. *Eur J Intern Med* 2011; **22**:172–176.

30 Minas M, Hatzogloua C, Karetsia E, Papaioannoua AI, Tanoua K, Tsarouchaa R, *et al.* COPD prevalence and the differences between newly and previously diagnosed COPD patients in a spirometry program. *Prim Care Respir J* 2010; **19**:363–370.

31 Sandelowsky H, Ställberg B, Nager A, Hasselström J. The prevalence of undiagnosed chronic obstructive pulmonary disease in a primary care population with respiratory tract infections – a case finding study. *BMC Fam Pract* 2011; **12**:122.

32 Wouters EF. Local and systemic inflammation in chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2005; **2**:26–33.

33 Clearfield MB. C-reactive protein: a new risk assessment tool for cardiovascular disease. *J Am Osteopath Assoc* 2005; **105**:409–416.

34 Gan WQ, Man SF, Sin DD. The interactions between cigarette smoking and reduced lung function on systemic inflammation. *Chest* 2005; **127**:558– 564.

35 Angrill J, Agusti C, de Celis R, Filella X, Rano A, Elena M, *et al.* Bronchial inflammation and colonization in patients with clinically stable bronchiectasis. *Am J Respir Crit Care Med* 2001; **164**:1628–1632.

36 Sethi S, Murphy TF. Infection in the pathogenesis and course of chronic obstructive pulmonary disease. *N Engl J Med* 2008; **359**:2355–2365.

37 Bari MR,Hiron MM, Zaman SM, Rahman MM, Ganguly KC. Microbes responsible for acute exacerbation of COPD. *Mymensingh Med J* 2010; **19**:576–585.