

Interim Report from Burden of Obstructive Lung Disease (BOLD Study) in Tehran: Prevalence and Risk Factors of Chronic Obstructive Pulmonary Disease

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Received: 11 March 2014

Accepted: 28 May 2014

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Background: Chronic Obstructive Pulmonary Diseases (COPD) is estimated to rank fifth in burden of disease and third in terms of mortality by 2020 worldwide. It is characterized by chronic inflammation and non-fully reversible airflow obstruction, causing structural changes in the lungs that can be demonstrated by a post bronchodilator FEV1/FVC ratio <70%.

Materials and Methods: The sampling frame of the current study was the population of Tehran, the capital of Iran with the current population of nearly 8.1 million. A stratified cluster sampling strategy with proportional allocation within strata was used in this study. The target population was all Tehran residents, aged 18 to 40 in one group and over 40 in another, in the year 2013. The stratification process of the sample according to the 22 municipal districts of Tehran city has been incorporated in the sampling process. Proportional to the number of households in the 22 districts, the appropriate number of clusters is weighted according to each district. The decision about the number of clusters is based on total sample size; mean household members; and logistical facilities for subject enumeration, transport, and examination.

Results: The overall COPD prevalence defined by the spirometric functional criteria was 10%, higher in men 12 (11.9%) than in women 15 (8.8%); the prevalence was significantly higher in subjects aged over 55 years ($P=0.001$). Only 10(3.7%) of these COPD patients had already been diagnosed by a physician. Of all subjects fulfilling the criteria for COPD according to the Burden of Obstructive Lung Disease (BOLD) guidelines (post bronchodilator FEV1/FVC<70%), 90(33.3%) had chronic productive cough, and 262(96.7%) had either long-standing cough, sputum production, recurrent wheeze, dyspnea, or attacks of shortness of breath.

Conclusion: Due to the small sample size at this stage of project, conclusions should be drawn with caution. In this first epidemiological report in Tehran about COPD, a moderate prevalence of the disease was determined, and a high percentage of this figure had not been diagnosed before by a physician.

Key words: Chronic Obstructive Pulmonary Disease, COPD, Iran, Symptoms

INTRODUCTION

COPD is estimated to rank fifth in burden of disease and third in terms of mortality by 2020 worldwide (1, 2). It is characterized by chronic inflammation and non-fully reversible airflow obstruction, causing structural changes

in the lungs that can be demonstrated by a post bronchodilator FEV1/FVC ratio <70% ("fixed ratio")(3).

Tobacco smoking was proven to be the most important risk factor for development of COPD (2); however, not all patients with COPD have a history of smoking. It seems

that about 50% of cases worldwide are related to smoking (4), and an estimated 10%–12% of individuals with COPD have never smoked (5). In other words, non-fully reversible airflow obstruction also occurs in never smokers. Iran is a developing country where the smoking rate (14.8%) is lower than the rate in many developed countries (6).

National estimations of COPD prevalence are mainly based on self-reported questionnaires without objective measurement of lung function like spirometry testing.

One survey of COPD in Isfahan estimated the prevalence rate to be 5.7% (7).

Different investigations, using spirometry, done in different countries have demonstrated under-diagnosis of COPD. One example was observed in Japan, where the results of a population-based study of the prevalence of COPD in 2004 were contrary to the estimates of the Japanese Ministry of Health (10.9% vs. 0.3%, respectively) (8). Similar rates of under-diagnosis have been frequently reported (9).

Considering the whole impact of COPD, it seems that this chronic disease fails to receive sufficient care from the health care community and governments and is rather unfamiliar to the public. A major problem seems to be the lack of information about the prevalence, distribution, and risk factors of COPD, especially in developing countries.

Evaluation of COPD prevalence definitely depends on the characteristics of sample population and criteria used in order to diagnose COPD, with continuing debate over the fixed spirometric ratio of 0.7 or lower limit of normal (10).

Academic institutions and governments consider conducting research on different aspects of COPD as important health priorities, because of its high prevalence in different regions (11) and because this disease seemed to be potentially preventable (12) by providing smoking cessation services, and air pollution control.

Since COPD causes mortality and morbidity, epidemiological and geographical data on COPD are limited to Eastern Mediterranean Region, including Iran.

The Burden of Obstructive Lung Disease (BOLD) Initiative was designed a decade ago to spread robust models that can be applied to different regions to estimate the prevalence as well as the current and future economic burden of COPD (13).

The goal of the present study was to report the prevalence and determine the main causes and risk factors of COPD in Tehran residents.

MATERIALS AND METHODS

Population and sampling strategy

Since 1976 Tehran Province includes seven cities and Tehran city is the biggest one amongst them. The sampling frame in this study was the population of Tehran city. According to the latest census, the present population of Tehran is nearly 8.1 million.

Sample Size

Given a design effect of 1.5, a prevalence rate of 11% in previous studies, and a response rate of 60%, total sample size was calculated to be 375. Considering this figure for both sexes, this value was calculated to be 750. In order to develop valid estimates of future burden of disease, researchers are determined to carry out an additional cohort on the prevalence of other key risk factors.

Sampling

A stratified cluster sampling strategy with proportional allocation within strata was used in this study. The target population was all residents, aged 18 to 40 in one group and over 40 in another, of Tehran city in the year 2013.

The stratification of the sample according to the 22 municipal districts of Tehran city was incorporated in the sampling process. Proportional to the number of households in the 22 districts, the appropriate number of clusters was weighted according to each district. The decision about the number of clusters is based on total sample size, mean household members, and logistical facilities for subject enumeration, transport, and examination.

For each cluster, a team of three members (one male and one female as interviewers dressed in white medical

coat and a driver) approached the index household specified via the aforementioned random selection of clusters, and continued the enumeration in 10 neighboring households in a systematic manner by proceeding round in a clock-wise direction. In the indexed household, if there was more than one person, the interviewers were advised to use Kish method to choose the right participant(s). The Kish Grid or method is a table of numbers, named after the statistician who invented it. The number of people in the household is found, and a random number is chosen to select a particular person.

Examination Protocol

The examination protocol included a questionnaire covering respiratory symptoms, health status, activity limitation, and exposure to potential risk factors, such as tobacco smoke, occupational risk factors, and biomass exposure. They also performed pre- and post-bronchodilator spirometry tests. Spirometry records provide the 1-second and 6-second forced expiratory volumes (FEV1 and FEV6) and the forced vital capacity (FVC).

Questionnaires

The core questionnaire was developed using pre-existing validated questionnaires that had already been used in multi-national studies (2). The questionnaire obtained information about respiratory symptoms, exposure to potential risk factors, including smoking, occupation, respiratory diagnoses, co-morbidities, health care utilization, medication use, physical activity limitation, and general health condition.

Participants were also expected to complete an occupational questionnaire and (for current cigarette smokers) a “stages of change” questionnaire that assessed readiness to quit smoking. There was also another questionnaire to assess exposure to biomass fuels used at home for either heating or cooking. All questionnaires were translated to Persian first and then back translated to English by a different translator. The questionnaires were administered by trained and certified staff; self administration of questionnaires was not allowed.

Spirometry

The single most important outcome measure obtained as part of this protocol was spirometry before and after administration of 200 mg (2 puffs) of salbutamol. To optimize quality control in this study, all teams were required to use the 2120 In2itive Vitalograph Spirometer, which was chosen because it provides an acceptable degree of accuracy, robustness, portability, and ease of storage. It can be used easily in this field and where there is no electricity. The 2120 In2itive Vitalograph Spirometer has been approved by the National Research Institute of Tuberculosis and Lung Disease to meet the predetermined performance criteria related to the reliability of measurement, suitability for field use, and ease of access to data.

Statistical analysis

In calculating standard errors and the 95% confidence interval for categorical and continuous variables, the cluster sampling design was taken into account and adjusted for. In addition to descriptive analyses, odds ratios were calculated with multivariate logistic regression in order to control potential confounding variables, and account for cluster design effects.

Materials and methods of this study have already been published elsewhere (14).

RESULTS

Participants

Up to the time of interim report, a total of 613 individuals were visited in five districts of Tehran; 267(43.6%) men and 346 (56.4%) women participated in the structured interviews. These five districts were (1, 4, 5, 10 and 15) located in north, south, west, east, and center; of Tehran. Of the lung function tests, 287 were included in the analyses, as 13 participants did not complete lung function tests satisfactorily. Table 1 shows the demographic characteristics.

Smoking habits

Overall, 104 (39.0%) men and 14 (4.0%) women had cigarette smoking experience ($P < 0.001$). These figures for

water pipe smoking experience were 120 (44.9%) for men vs. 48 (13.9%) for women ($P < 0.001$). Regarding the age of starting smoking, men started at younger ages (20.77 ± 6.84 yrs.) than women (23.21 ± 7.23 yrs.) ($P = 0.05$).

In this sample, 118 (19.2%) were ever smokers, 168 (27.4%) were water-pipe ever smokers, and 8.0% were cigar or pipe ever smokers. For current-smokers, 27 (38.0%) had dual addiction to cigarette and water pipe.

Table 1. Demographic characteristics

	Subjects, No.	%
Gender		
Male	267	43.6
Female	346	56.4
Age Yr*		
18-39	313	51.1
≥ 40	300	48.9
Districts		
1	101	16.5
4	195	31.8
5	140	22.8
10	69	11.3
15	108	17.6
Smoking status		
Non-smoker	498	81.2
Ex-smoker	44	7.2
Current smoker	71	11.6
Male	61	85.9
Female	10	14.1

Respiratory symptoms

Respiratory symptoms in all subjects

In this study's population, the most commonly reported respiratory symptoms were: sputum production

in 179 (29.2%) (95% CI: 25.6%-32.8%), chronic cough in 163 (26.6%) (95% CI: 23.1%-30.1%), and wheezing in 123 (20.1%) (95% CI: 16.9%-23.2%). As for dyspnea, 53 (8.6%) (95% CI: 6.4%-10.9%) of participants had this symptom during the past year.

Respiratory symptoms in subjects with COPD

Among 271 individuals, the prevalence of COPD was 10% (95% CI: 6.4%-13.6%), according to the GOLD standards. Only 10 (3.7%) of these COPD patients had already been diagnosed by a physician. Of all subjects fulfilling the criteria for COPD according to BOLD guidelines (post bronchodilator $FEV_1/FVC < 70\%$), 90 (33.3%) had chronic productive cough, and 262 (96.7%) had either of long-standing cough, sputum production, recurrent wheeze, attacks of shortness of breath, or dyspnea. Furthermore, according to the survey only one person among those who had $FEV_1/FVC < 70\%$ (3.7% of labeled people) was diagnosed with chronic bronchitis, emphysema, or COPD by the healthcare system while this figure for the whole population was 20 (3.3%) (Table 2).

The overall COPD prevalence defined by the spirometric functional criteria was 10%, higher in men 12 (11.9%) than in women 15 (8.8%); the prevalence was significantly higher in subjects aged over 55 years ($P = 0.001$).

COPD distribution is presented in Table 3 according to the socio-demographic characteristics. There were significant differences among the subgroups.

Table 2. COPD prevalence according to age, gender, and COPD definition criteria*

Age, yr	Spirometry: Postbronchodilator FEV ₁ /FVC < 70%			COPD definition criteria Medical: Prior medical diagnosis			Clinical: Chronic bronchitis		
	Female	Male	Total†	Female	Male	Total	Female	Male	Total††
<55	4 (2.4)	3 (3.0)	7 (2.6)	3 (1.8)	1 (1.0)	4 (1.5)	30 (16.0)	17 (15.0)	47 (15.7)
≥ 55	11 (6.5)	9 (8.9)	20 (7.4)	4 (2.4)	3 (3.0)	7 (2.6)	16 (8.6)	4 (3.5)	20 (6.7)
Total	15 (8.9)	12 (11.9)	27 (10)	7 (4.1)	4 (4.0)	11 (4.1)	46 (24.6)	21 (18.6)	67 (22.3)
95% CI	4.6-13.2	7.0-16.8	6.4-13.6	1.1-7.1	1.0-7.0	1.7-6.5	19.7-29.5	14.2-23.0	17.6-27

*Data are presented as No. (%) unless otherwise indicated.

† Within participants aged over 40 with successful Spirometry (270)

†† within participants aged over 40 (300)

Table 3. COPD distribution according to the socio-demographic and disease characteristics

Characteristics	No COPD (n = 244)	COPD (n = 27)	95% CI	Total (n = 271)
Region				
1	97.6%	2.4%	0-7.2%	42
4	87%	13%	6.0-20.1%	92
5	87.5%	12.5%	4.2-20.8%	64
10	90%	10%	0-21.4%	30
15	93%	7%	0-14.9%	43
Gender				
Male	88.1%	11.9%	5.5-18.3%	101
Female	91.2%	8.8%	4.5-13.1%	170
Age group				
<55 years	95.5%	4.5%	1.2-7.9%	154
≥55 years	90%	10%	10.3-24.2%	116
Education				
Illiterate	100%	0%	---	1
<5 years of school	85.3%	14.7%	7.7-21.7%	102
5–12 years of school	91%	9.0%	3.6-14.2%	111
University education	96.5%	3.5%	0-8.4%	57
Body mass index				
Normal weight	78.3%	21.7%	10.9-32.4%	60
Overweight & obese	93.3%	6.7%	3.3-10.1%	209

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease.

Among smokers, the prevalence of COPD according to GOLD was 16.3% (95% CI: 5.1-12.5%) and in non-smokers this rate was 8.8% (95% CI: 4.8-27.8%) ($P = 0.161$).

Cronbach's alpha for spirometry variables was 74.1%.

In multivariate analysis when including age, gender, smoking habits, and geographical districts in the model, age appeared to be a risk factor. COPD according to GOLD criteria as the dependent variable yielded an odds ratio (OR) of 1.1 for the age over 40.

DISCUSSION

In this study, we estimated the prevalence of COPD using questionnaires and spirometry amongst people aged 18 years and older living in Tehran. The sample in this interim report was representative of Tehran adult population and the participation rates were exceptionally high for comprehensive surveys like this. The greater percentage of women in this study (56.4%) cannot be

explained by the composition of the population in Iran which is nearly equal between genders (15); but, mainly, by the cultural trait that women spend more time at home than men. The same essential questions on risk factors were asked about tobacco smoking and previous illnesses diagnosed by a physician (including asthma) in the survey.

COPD prevalence in Tehran was within the range reported in other countries like China (Guangzhou), and Philippines (Manila), but is lower than the observed prevalence in South Africa (Cape Town), Australia (Sydney), and Turkey (Adana) (16).

According to a study done in Isfahan, another metropolitan of Iran, the prevalence of airflow limitation in the general population 40 years and older was 5.7% (7), but in our study, the prevalence of COPD in people over 40 years of age was higher. There seems to be a lack of relevant longitudinal studies, conducted locally, whereas in other countries, e.g. Vasankari et al comparing

prevalence of COPD throughout a decade, found no increase in the prevalence rate in Finland, (17) and Soriano et al. found an unexpected decrease in COPD prevalence in Spain (18). The data from the current study will be available as a baseline tool for future studies of chronic obstructive pulmonary disease.

There is an unfinished discussion on how to improve early diagnosis of COPD. In this report, we found a high prevalence (5.9%) of previously undiagnosed COPD. The stepwise and slow progressive nature of COPD means that most sufferers tend not to complain of respiratory symptoms and consequently the disease usually remains undetected by health providers for many years. Moreover, an insufficient distribution of spirometers in all clinics may influence the prevalence of undiagnosed COPD cases. Another reason for the rate of undiagnosed patients seems to be physicians' and patients' attitudes. Studies have shown that under-diagnosis of COPD is increasing partly due to "physicians' delay", i.e., doctors who do not suspect underlying COPD (18, 19) and partly because of "patient's delay in seeking treatment", i.e., patients who self-report good health (20).

It seems that, primary screening for airflow obstruction with a handheld spirometer prior to full spirometry testing which is easy to carry in all settings, could be considered as an efficient way of screening or finding new COPD cases (21).

In conclusion, we demonstrated that there are possibly a number of cases of undiagnosed COPD by general physicians in Tehran. However, the early stages of COPD are difficult to diagnose without spirometry. Actually, spirometry is not widely used among Iranian general physicians. This study suggests that general clinics must be equipped with spirometer in order to reduce the number of undiagnosed COPD cases. This is particularly relevant when evaluating the respiratory function of individuals with clinical signs of airflow obstruction.

In this study, we found that the prevalence of airflow limitation was higher in ever smokers, which is the same as that in previous reports (22).

Besides, the prevalence of airflow limitation was similar in current smokers and former smokers, which suggests the need for effective smoking cessation programs that impact individuals earlier in their smoking histories. However, even for those individuals who have already developed COPD, smoking cessation is clearly an intervention that has been proven to play a role in preventing the progression of disease (23, 24).

Considering these findings, early detection of COPD is important for early smoking cessation intervention and the administration of beta-agonists and inhaled corticosteroids.

The current study may be subject to several biases: Although a weighting procedure was performed to make the sample as representative as possible, there was still a possibility of a selection bias because there was no means to evaluate the reasons of rejection, which could have led to an overestimation or underestimation of the COPD prevalence. The authors of this study assume that refusals were linked to cultural traits, lack of motivation, illiteracy, or maybe due to chronic conditions that individuals did not want to disclose (cancer or other diseases). There is also a possibility of an information bias in this study: as in all studies requiring questionnaires, relying on individuals reporting different variables may include a recall bias (previous exposure data for example) or subjectivity bias (weight, height, symptoms reporting for example). Moreover, portable spirometers may not be sufficiently sensitive and specific and may result in a classification bias. However, the methods used in this study are the ones that are currently being used in a large number of countries all over the world for this kind of study. Although improved methods may help improve the accuracy of this kind of study, the authors believe that this evolution will not be of major importance.

CONCLUSION

Due to the small sample size at this stage of the project, conclusions should be drawn with caution. In this first epidemiological report in Tehran about COPD, a moderate prevalence of the disease was determined, and a high percentage of this figure had not been diagnosed before by a physician. In this study, older individuals seemed to have an increased risk of COPD, and this fact ran in “ever” smokers. Accordingly, prevention campaigns including smoking cessation clinics and facilities should cooperate to reduce prevalence, morbidity, and mortality of COPD. Thus, it is important for health professionals to identify high-risk groups for chronic respiratory diseases and refer them for spirometry testing for early detection of COPD.

Disclosure

The authors report no conflicts of interest in this work.

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