Original Article

Burden of Obstructive Lung Disease in Iran: Prevalence and Risk Factors for COPD in North of Iran

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Abstract

Background: Globally chronic obstructive pulmonary disease (COPD) was reported as the fourth leading cause of death (5.1%) in 2004 and is projected to occupy the third position (8.6%) in 2030. The goal of the present project is to describe the prevalence and risk factors of COPD in a province in the north of Iran. **Methods:** This study followed a stratified cluster sampling strategy with proportional allocation within strata. The stratification of the sample according to the 31 provinces of Iran is incorporated in the sampling process. The single most important outcome measure obtained as part of this protocol was spirometry before and after the administration of 200 mg (2 puffs) of salbutamol. The descriptive statistics for categorical variables included the number and percent and for continues variables included the mean ± SD. **Results:** A total of 1007 subjects were included in the study. Among all participants, 46 (5%) subjects had COPD on the basis of symptoms and 43 (8.3%) subjects had COPD on the basis of spirometry criteria. In univariate analysis, urban inhabitants in comparison with rural inhabitants had lower COPD risk (OR: 0.48; 95% CI: 0.24–0.95), smoker had higher risk compared with nonsmokers (OR: 1.97; 95% CI: 1.01–3.82), and subjects with exposure to dust (OR: 2.07; 95% CI: 1.09–3.94) had higher risk compared with contrary status. **Conclusions:** This study showed that occupational and environmental smoke exposure was associated with COPD. A new design of preventive measures must be taken to control cooking energy and cooking stoves, particularly in rural areas.

Keywords: *Airway obstruction, burden of obstructive lung disease, Iran, prevalence*

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease with an increasing prevalence worldwide, especially in developing countries.[1] COPD is a global health burden that affects 300 million people worldwide resulting in >3 million deaths annually.[2,3] Globally COPD was reported as the fourth leading cause of death (5.1%) in 2004 and is projected to occupy the third position (8.6%) in 2030. A majority of COPD-related deaths occurs in low- and middle-income countries.[4] In 2010, it was said that above 230 million people living in urban areas (prevalence of 13.6%), and >153.7 million people living in rural areas (prevalence of 9.7%), were affected by COPD.[5] In published studies, the prevalence of COPD has been reported as a considerable range of estimates across different countries. This rate was reported between 0.2% in Japan and 37% in the USA.[6] It is said that merely around one-fourth of cases are diagnosed at the early stages.[7] COPD is characterized by chronic inflammation and non-fully reversible airflow obstruction, involving structural changes in the lung that can be demonstrated as a low ratio (<0.7) of forced expiratory volume in 1 s (FEV1) to forced vital capacity (FVC).[7,8]

Various risk factors of COPD in developing countries likely differ from those in developed ones. Although tobacco smoking rates are different in these countries, exposure to biomass fuels, cooking indoors, high tuberculosis prevalence, and different age structure have a relevant influence on COPD epidemiology.[9] According to World Health Organization report 2014, one-third of the world's population were using biomass fuel, including wood, crop residues, such as straw and sticks, dried leaves, twigs, wild grass, animal dung, or charcoal, for cooking and/or heating.[10] The smoke from these biomass fuels had a clear roll in the incidence of COPD.[11]

Smoking and exposure to environmental tobacco smoke have been proved to be the

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strongest risk factors for airflow obstruction,[12] but many areas of the world with high mortality rates from "COPD" still have low consumption of tobacco, implying that tobacco smoking alone does not explain the distribution of COPD.[13-15] In our previous studies, we found that the prevalence of airflow limitation was higher in individuals who had ever smoked or been passive-smoker,[16,17] but was prevalent in never-smokers as well. Iran is a developing country where the smoking rate is lower than in many developed countries.[18]

It has been proved that 90% of COPD deaths occur in developing countries in the future and 40% of these deaths are attributable to tobacco smoking, notwithstanding a high prevalence of COPD in some of developing countries.[19] The burden of COPD in developing countries seems to be high because of several reasons including challenges with COPD diagnosis, increased exposures to risk factors, relatively low COPD awareness, and combustion products of biomass fuels.[20]

The international, population-based Burden of Obstructive Lung Disease (BOLD) Initiative was designed to develop robust models during last 2 decades, which can be used to estimate the prevalence and current and future economic burden of COPD.[21] It is undoubtedly crucial that geographic distribution and variation of COPD occurrence provide national data for quality of public health activities and clinical health care services.

The objectives of this study were to estimate the prevalence, clinical characteristics, disease severity, previous physician diagnosis, management of COPD, and a comparison of urban and rural communities in Mazandaran Province, Iran.

Methods

The BOLD study protocol in Iran was published elsewhere.[22]

Population and sampling strategy

We used the same sampling protocol consistently throughout the project. The sampling frame in this study was the whole population of Mazandaran Province located in the north of Iran. The present population in this area was ~3 million.

Sample size

Drawing upon our experience, a design effect of 1.5, prevalence rate of 50%, and a response rate of 90%, the total sample size was calculated by 385 in 2 different sexes for ≥40 years of age, and 385 for 18–39 years.

Sampling plan

This study followed a stratified cluster sampling strategy with proportional allocation within strata. The target population was all noninstitutionalized inhabitants, aged 18–40 in one group and >40 in another, who inhabited in urban or rural areas of Mazandaran in 2016.

The stratification of the sample according to the 19 cities of Mazandaran Province was incorporated in the sampling process. The appropriate number of clusters was weighted according to each city. The decision about the number of clusters was on the basis of total sample size; mean household members; and logistical facilities for subject enumeration, transport, and examination.

For each cluster, a team of 3 members (1 male and 1 female aged <28 as interviewers dressed in white medical overall and a driver) approached the index household, which was specified through the aforementioned random selection of clusters, and continued the enumeration in 10 neighbor households in a systematic manner by proceeding round in a clockwise direction. In an indexed household, if there was >1 person, then interviewers were advised to use the Kish method to choose the right participant(s).[23]

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 postbronchodilator spirometry tests. Spirometry records provide the 1-s and 6-s forced expiratory volumes (FEV_1 and FEV_6) and the FVC.

Questionnaires

The Core questionnaire was developed from pre-existing validated questionnaires that had already been used in multinational studies.[1] The questionnaire obtains information about respiratory symptoms, exposure to potential risk factors, including smoking, occupation, respiratory diagnoses, comorbidities, health care utilization, medication use, activity limitation, and health status.

Participants also were 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 a questionnaire to assess exposure to biomass fuels used in the 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 the field and where there is no electric power available. The 2120 In2itive Vitalograph Spirometer had been approved by National Research Institute of Tuberculosis and Lung Diseases as meeting predetermined performance criteria relating to the reliability of measurement, suitability for field use, and ease of access to data.

COPD definitions

COPD definitions were: (1) spirometry: postbronchodilator FEV1/FVC ratio <70%; (2) prior medical diagnosis: an affirmative response to: "Have you ever had chronic bronchitis, emphysema, or COPD confirmed by a doctor?"; and (3) clinical definition: positive criteria for the standard definition of chronic bronchitis. These definitions allowed comparison without any need for reference values and were a widely used standard that can be compared with other published studies.[8,24]

Humanity and ethics

The study has been approved by the Research and Ethics Committee of Shahid Beheshti University of Medical Sciences and Ethics Committee of National Research Institute of Tuberculosis and Lung Disease since 2014.

Statistical analysis

The descriptive statistics for categorical variables were included the number and percent and for continues variables were included the mean ± SD. The prevalence was calculated by proportion and compared by the χ^2 test. To evaluate the factor associated with COPD by criteria, univariate and multivariate logistic regression analyses were performed. All statistical analyses were performed by SPSS 19 software and 0.05 was considered as significant level.

Results

Demographic information

A total of 1007 subjects were included in the study. Among under study participants, 500 (49.7%) subjects were males and 507 (50.3%) were females. The mean age of participants was 44 ± 14.16 years and their other characteristics are presented in Table 1.

Table 1: Demographic and social characteristics of the study population

	Number	%
Age group		
<40	459	46.8
≥40	522	53.2
Gender		
Male	500	49.7
Female	507	50.3
Region		
Urban	514	51
Rural	493	49
Education		
Less educated	107	10.6
Primary school	123	12.2
Secondary school	490	48.7
University	286	28.4
Smoking status		
Never smoker	778	78.3
Current smoker	219	21.7
Exposure to dust and fumes at workplace		
Yes	383	38.2
No	621	61.7
Chronic bronchitis (chronic cough and sputum)		
Yes	110	10.9
No	897	89.1
Self-reported asthma		
Yes	56	5.6
No	950	94.4

COPD and symptoms

There are 266 (26.4%) subjects with dyspnea including *123 (48.1%) in villages and 143 (51.9%) in cities, 200 (19.95%)* with chronic cough (51.5% in cities and 48.5% in villages), and 220 (21.8%) with sputum production (48.2% in cities and 51.8% in villages). Among all participants, only 5 (0.5%) subjects had a prior medical diagnosis of COPD, 46 (5%) subjects had COPD on the basis of symptoms and 43 (8.3%) subjects had COPD on the basis of spirometry criteria. The frequency distribution of subjects according to the latter diagnosis criteria by demographic and also potential important factors are presented in Table 2. Exposure to dust and fumes at workplace rates was higher in rural areas than in urban areas *(47 (9.6%) vs 28 (5.4%), $P < 0.0001$)*. The rates of having an open fire with wood, crop residues or dung as a primary means of heating your home for >6 months, and of cooking were both higher in rural areas areas *(106 (21.5%) vs 87 (16.9%) $P < 0.0001$ and 116 (23.6%) vs 89 (17.4%) $P < 0.0001$, respectively)*.

The prevalence of COPD on the basis of symptoms in males (58.7%) was similar to females (41.3%) ($P = 0.19$) and in the over 40 years of age (65.1%) was more than the under 40 years of age (34.9%) ($P = 0.04$). The prevalence

Table 2: The frequency of COPD* on the basis of defined criteria

	COPD on the basis of symptom		COPD on the basis of FEV_1/FVC <0.7	
	With COPD *n* (%)	Without COPD *n* (%)	With COPD *n* (%)	Without COPD *n* (%)
Age group				
<40	15 (34.9)	425 (49.7)	1 (2.4)	13 (2.8)
≥40	28 (65.1)	430 (50.3)	41 (97.6)	455 (97.2)
Gender				
Male	27 (58.7)	437 (49.8)	22 (51.2)	237 (50.2)
Female	19 (41.3)	440 (50.2)	21 (48.8)	235 (49.8)
Region				
Urban	21 (45.7)	445 (50.7)	15 (34.9)	251 (53.2)
Rural	25 (54.3)	432 (49.3)	28 (65.1)	221 (46.8)
Education				
Less educated	7 (15.2)	82 (9.4)	14 (32.6)	86 (18.2)
Primary school	7 (5.3)	99 (11.3)	9 (20.9)	91 (19.3)
Secondary school	25 (54.3)	425 (48.5)	14 (32.6)	196 (41.5)
University	7 (15.2)	270 (30.8)	6 (14.0)	99 (21.0)
Smoking status				
Never smoker	28 (60.9)	692 (78.9)	28 (65.1)	371 (78.6)
Current smoker	18 (39.1)	185 (21.1)	15 (34.9)	101 (21.4)
Self-reported asthma				
Yes	12 (26.7)	38 (4.3)	3 (7)	32 (6.8)
No	33 (73.3)	839 (95.7)	40 (93)	439 (93.2)
Exposure to dust and fumes at workplace				
Yes	27 (58.7)	320 (36.6)	27 (62.8)	212 (44.9)
No	19 (41.3)	554 (63.3)	16 (23)	260 (55.1)
Chronic bronchitis (chronic cough and sputum)				
Yes	46 (100)	52 (5.9)	11 (25.6)	60 (12.7)
No	0 (0)	825 (94.1)	32 (74.4)	412 (87.3)

COPD=Chronic obstructive pulmonary disease; FEV_1=Forced expiratory volume in 1 s, FVC=Forced vital capacity.

of COPD on the basis of spirometry in males (51.2%) and females (48.8%) was nearly the same (P = 0.88) and in over 40 years (97.6%) was more than the under 40 years (2.4%) (P < 0.001). The prevalence of COPD on the basis of symptoms among the urban areas (45.7%) and the rural areas inhabitants (54.3%) was approximately the same (P = 0.55). On the basis of spirometry, the prevalence of COPD among the urban areas inhabitants (34.9%) was less than the rural areas (65.1%) (P = 0.02).

Factor associated with COPD

According to univariate logistic regression, the risk of COPD on the basis of symptoms in current smokers was more than never-smokers (OR: 2.40; 95% CI: 1.30–4.44) and in urban inhabitants is less than rural inhabitants (OR: 0.48; 95% CI: 0.24–0.95). Subjects with exposure to dust and fumes at the workplace had a higher risk of COPD compared with subjects without exposure (OR: 2.46; 95% CI: 1.35–4.50). According to multivariate analysis, current smokers (OR: 1.93; 95% CI: 1.02–3.67) and subjects with exposure to dust (OR: 2.07; 95% CI: 1.09–3.81) had significantly higher COPD risk.

For COPD diagnosed by spirometry in the univariate analysis, urban inhabitants in comparison with rural inhabitants had lower COPD risk (OR: 0.48; 95% CI: 0.24–0.95)). Subjects who were smoker had a higher risk compared with subjects who were not (OR: 1.97; 95% CI: 1.01–3.82). The risk of COPD for subjects with exposure to dust (OR: 2.07; 95% CI: 1.09–3.94), subjects with chronic bronchitis (OR: 2.36; 95% CI: 1.13,4–93) and subjects with asthma (OR: 8.03; 95% CI: 3.84–16.77) was higher compared with its contrary status. In the multivariate analysis, no significant association was found [Table 3].

Discussion

The present cross-sectional survey of 1007 adults was the first systematic epidemiological study of COPD prevalence and risk factors comparing urban and rural communities in Iran. The estimates of risk factors presented here were on the basis of the age range starting from 18 years, and spirometric screening of COPD was on the basis of people aged ≥40 years. All participants were living in 19 different cities and 19 villages near the main cities.

The study showed that the prevalence of previously diagnosed COPD reported by respondents was 0.5%, and the total prevalence according to the global initiative for chronic obstructive lung disease criteria was 8.3% (95%

Table 3: Factor associated with COPD using logistic regression

	COPD on the basis of symptom		COPD on the basis of FEV_1/FVC <0.7	
	Univariate	Multivariate	Univariate	Multivariate
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age group				
<40	1		1	
≥40	(0.97-3.50)		1.17 (0.15-9.18)	
Gender				
Male	1		1	
Female	0.70 (0.38-1.27)		0.96 (0.51-1.79)	
Education				
Less educated	1		1	
Primary school	0.82 (0.28-2.46)		0.61 (0.25-1.48)	
Secondary school	0.69 (0.29-1.65)		0.44 (0.20-0.96)	
University	0.30 (0.10-0.89)		0.37 (0.14-1.01)	
Region				
Urban	0.48 (0.24-0.95)	0.87 (0.48-1.59)	0.48 (0.24-0.95)	0.53 (0.27-1.02)
Rural	1	1	1	1
Smoking status				
Never smoker	1	1	1	1
Current smoker	2.40 (1.30-4.44)	1.93 (1.02-3.67)	1.97 (1.01,3.82)	1.66 (0.82-3.29)
Exposure to dust and fumes at workplace				
Yes	2.46 (1.35-4.50)	2.07 (1.09-3.81)	2.07 (1.09-3.94)	1.67 (0.5-3.27)
No	1	1	1	1
Chronic bronchitis (chronic cough and sputum)				
Yes			2.36 (1.13-4.93)	2.01 (0.92-4.40)
No			1-	
Self-reported asthma				
Yes	1.03 (0.30-3.51)		8.03 (3.84-16.77)	0.71 (0.19-2.60)
No	1		1	1

CI=Confidence interval; COPD=Chronic obstructive pulmonary disease, OR=Odds ratio

CI: 6.26%–11.06%). This difference has proved the benefit of spirometric screening of COPD using the postbronchodilator fixed ratio of FEV_1/FVC <0.7 as a discriminating criterion.[21,25] The observations from this study were similar to the results found in many other countries with an expected range of 4%–10% using spirometry,[24,26] though it was higher compared with previously reported findings from Western Pacific and South East Asia.[27,28] This figure is considerably close to our previous results in Iran.[16,17]

Mazandaran Province has diverse nature stretching from the sandy beaches of the Caspian Sea to the rugged and snowcapped Alborz sierra. Although this region experiences windy climate but is known as one of the most densely populated. However, the exact impression of these assumptions needs further investigation.

In this study, rural residents had significantly higher rates of COPD on the basis of spirometry than urban residents. These differences could be because of socioeconomic variations between urban and rural areas that provide unequal opportunities to improve participants' standard of living. A meta-analysis by Adeloye *et al*. revealed that across world regions, urban dwellers had higher COPD prevalence rates (13.2%; 95% CI: 11.8%–14.7%) than rural populations (10.2%; 95% CI: 8.2%–12.2%),[1] and over a period of 20 years between 1990 and 2010, the percentage of rise in COPD cases was higher among urban inhabitants than among rural residents.

The relationship between lung health status and habitation location is complex and depends on factors such as; occupational exposures, lifestyle, and differences in access to health care.[29]

Results of our investigation suggests a significant relationship between exposure to dusts and fumes at workplace, having an open fire with wood, and using crop residues or dung as a primary means of heating or cooking with the prevalence of COPD in urban and rural areas, like some studies in this field,[30,31] We did not find any differences between tobacco smoking in rural and urban areas, but rural residence were more exposed to other environmental and occupational risk factors for COPD such as fuel-fired power plants and agricultural work. Moreover, rural communities had a higher proportion of older inhabitants, which could explain higher rates of COPD in these participants. Jackson *et al*.[32] found higher hospitalization rates among rural compared with urban

inhabitants. Abrams *et al*. revealed higher mortality among veterans living in isolated rural areas likewise.[33]

In this study, the rate of COPD diagnosed by spirometry, and on the basis of symptoms, had a tendency to increase with age. This phenomenon could be explained by the physiological decrease in lung function and greater exposure to environmental and occupational risk factors with age. Brachier *et al*.[34] did not find any association between chronic bronchitis and increasing age in a study conducted in Pune slums in India. Our finding similar to a large number of previous epidemiological studies showed a high prevalence of COPD in the elderly and the rate of COPD sufferers had a gradual increase with increasing age.[25,26,35]

Prevalence of tobacco smoking in our study was similar to previous researches.[18] A statistically significant relationship was shown between smoking and COPD similar to previous reports.[24,26,27,36] The risk of COPD depends on the number of consumed cigarettes and the duration of smoking. It has been proved that any amount of tobacco is harmful, although the risks could be lower at low quantity.[37] Chhabra *et al*. showed that the prevalence of chronic respiratory diseases among smokers with >2.5 pack-years was higher.[38] Similarly, Mahesh *et al*. reported that prevalence of COPD in smokers with <20 pack-years was 9.6%, which increased to 18% in subjects who smoked >20 pack-years.[39] It seems that there is a strong relationship for cigarette smoking and COPD, with no evidence of a threshold. Interestingly, in our study, around two-thirds of COPD participants were never-smokers. There was increasing evidence on the occurrence of COPD in nonsmoking individuals showing an estimation of 25%–45% of patients with COPD have never smoked tobacco.[13] The rate of COPD in never-smokers suggests that, besides tobacco smoking, other risk factors such as genetic factors, impaired lung growth, infections and environmental exposures including occupational exposures and (outdoor and indoor) air pollution might contribute to the development of COPD.[13,40]

The strengths of this study were similar to other BOLD studies across the world enjoying a population-based sampling frame derived from 19 different cities and 19 different villages in a province and collecting data. In addition, measurements of the variables in this study were done independently of the research question, which made it less prone to information and selection bias.

Conclusions

In conclusion, these results added to the growing literature on geographic disparities among patients with COPD and provided evidence that the prevalence of COPD, in general, tends to be higher in the rural community. However, both rural and urban groups were equally underdiagnosed and undertreated.

This study showed that occupational and environmental smoke exposure was associated with COPD. A new design of preventive strategies especially must be done to cooking energy and cooking stoves, particularly in rural areas.

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Conflicts of interest

There are no conflicts of interest.

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