Prevalence of Chronic airflow limitation in Kashmir, North India: Results from the BOLD study.

Running title: CAL in north India, the BOLD study.

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Abstract:

Background: Data on spirometrically defined chronic airflow limitation (CAL) are scant in developing countries. We set out to estimate the prevalence of spirometrically defined CAL in Kashmir, North-India.

Methods: Using BOLD survey methods, we administered questionnaires to randomly selected adults aged ≥ 40 years. Post-bronchodilator spirometry was performed to estimate the prevalence of CAL and its relation to potential risk-factors.

Findings: From 1100 participants initially recruited, 953 (86.9%) responded, 757 completed acceptable spirometry and completed questionnaires. The prevalence of an FEV1/FVC ratio less than the lower limit of normal was 17.3% (4.5) in men and 14.8% (2.1) in women. Risk factors for CAL included higher age, cooking with wood, and a lower educational status. The prevalence of current smoking was 61% in men and 22% in women; most smoked hookahs. CAL was found equally in non-smoking males and females and was independently associated with use of hookah, a family history of respiratory disease and poor education. A self-reported doctor's diagnosis of COPD was reported in 8.4/1000 (0.9% in women and 0.78% in men).

Interpretation: Spirometrically-confirmed CAL is highly prevalent in Indian Kashmir and seems related to high prevalence of smoking, being predominantly in the form of hookah smoking.

Introduction:

Chronic obstructive pulmonary disease (COPD), a disorder of chronic airflow limitation (CAL) not reversed by bronchodilators, is now the 3rd most common cause of death worldwide.[1] While most of the information on COPD prevalence and morbidity comes from high-income countries, it is known that low- and middle-income countries already shoulder much of the burden of COPD mortality with almost 90% of COPD deaths taking place in these countries.[1] While previous estimates of prevalence have used self-reported doctor-diagnosis of COPD, the routine use of spirometry has shown a wide gap between these estimates and the actual burden as a result of under-diagnosis.[2-7]

Data from the Indian subcontinent are sparse and mostly based on questionnaire surveys.[8-12] Crude estimates suggest that there are about 30 million COPD patients in India,[10] with prevalence rates ranging from 2 to 22% in men and 12 to 19% in women. In a recent country wide questionnaire-based survey in India, the prevalence of chronic bronchitis was reported as 3.49% in adults $\geq$ 35 years of age (median prevalence of 4.27% in men and 2.7% in women).[10] The only spirometry based study from India has reported a nearly 2-fold higher prevalence,[11] suggesting that the true burden is much higher than the reported burden.[12]

The Burden of Obstructive Lung Disease (BOLD) study[13] measures COPD prevalence in multiple countries based on standardized, quality-controlled post-bronchodilator spirometry. The present study was designed to measure the prevalence of COPD in Kashmir, north India using the BOLD protocol.

Methods:

Study Population

We surveyed a gender-stratified random sample of the inhabitants of Hajan(Bandipora), Kashmir who were ≥ 40 years of age. Participants were selected from available information with the Census department of the Jammu and Kashmir (J&K) state. The survey was conducted on the non-institutionalised residents of the Bandipora district (population: 210,017). Five of the 115 regions that make up Bandipora district (Dangerpora, Hajan, Madwan, Nesbal and Sumbal), were selected and random samples of sub-regions were used within each region to select the final sex stratified sample for the study. The population of rural Kashmir is almost entirely Muslim with approximately 54% male.

We used the BOLD protocol to design and complete the study using trained and certified personnel .[14] All data collected were quality-controlled on a weekly/bi-weekly basis by the BOLD coordinating centre in London. Following an initial house visit, the potential participants were contacted by phone/in person to schedule a visit to the participant's home. For all subjects contacted, answers to a minimal data questionnaire were obtained. Of the 1100 individuals whom we attempted to contact, 3 were untraceable, 2 were unreachable and 12 had permanently moved from the area. Of the remaining 1083 eligible participants, 953 (88%) completed the full protocol and performed spirometry (responders). Of those, 757 performed acceptable spirometry and constitute the sample for this analysis.

Study Methodology

A team from the BOLD coordinating centre team from London trained and certified the staff at Pune in February, 2010. Questionnaires were translated from English into Kashmiri, then back-translated into English by independent translators, according to the International Quality of Life Assessment (IQOLA) protocol. The back translation was then compared with the original English versions for accuracy and then piloted in 10 volunteers. Questionnaires were administered to study participants in their native language through face-to-face interviews. Information was recorded for respiratory symptoms, smoking, other risk factors for COPD, health status, medication use, health-care utilization, comorbidities, respiratory diagnoses, and physical and mental quality of life (Short Form-12 questionnaire, Quality Metrics, Lincoln, RI, USA). [15] The other risk factors for COPD considered here include type of cooking fuel, the use of kangris (an earthenware pot with live wood-charcoal cinders carried inside a long robe called 'Phiran' for warmth), a history of tuberculosis, education and body mass index. Spirometry was performed according to ATS criteria, [16] using the Easy-One portable spirometer (ndd Medizintechnik; Zurich, Switzerland) with participants in a seated position. Separate measurements were made before and at least 15 min after two puffs of salbutamol (200 μg) administered via metered-dose inhaler with a double valve volumatic spacer (Zerostat spacer, Cipla Limited, India). Spirometry data were transmitted electronically to the BOLD Pulmonary Function Reading Centre in London where each spirogram was reviewed. A usable spirometry had to meet ATS criteria for acceptability included having at least three trials, two of which were acceptable (*i.e.*, free from artifact, sudden stops, and back-extrapolated volumes of > 5.0% of FVC) with the difference between the largest and second largest values being < 200 mL for both FEV_1 and FVC.[17] The spirometer was calibrated daily with a 3l syringe and the study staff was continuously monitored. Whenever technicians' quality scores dropped below a preset level, they had to stop conducting testing and be retrained and recertified. [14]

Definitions

The US National Health and Nutrition Examination Study (NHANES) III Caucasian reference equations[18] were used to calculate the lower limit of normal and the percent predicted values for the primary analysis. The lower limit of normal is the value exceeded by 95% of the "normal" population defined as asymptomatic life-time non-smokers. We report COPD stage 1 or higher defined by the lower limits of normal (LLN) for post-BD FEV_1/FVC based on the NHANES Caucasian reference equations for age and sex. Post-BD FEV1 <80% of the predicted was further used for COPD stage 2 or higher.

Doctor-diagnosed COPD was defined as self-reported physician's diagnosis of chronic bronchitis, emphysema, or COPD.

The number of self-reported pack-years of cigarettes smoked was defined as the average number of cigarettes smoked per day divided by 20 (*i.e.*, packs per day) times the duration of smoking in years. An equivalent value for pipefuls of tobacco smoked from a hookah was taken from the Smoking Pack Years Calculator.[19]

Education was divided into none, primary and above primary education.

Analysis

Prevalence estimates were calculated for the overall Hajan population, as well as for subgroups defined by gender and either age or "pack-years" or equivalent of smoking, using survey weights. These analyses were done using Stata 12 software. Mean FEV_1/FVC was estimated for sex and 10-year age groups. The proportion of participants with a low FEV1/FVC ratio compared to the 95th centile of the values reported by the NHANES "normal" Caucasian population was also calculated and reported for the same age groups. In order to adjust for the expected decline in the ratio with age the FEV1/FVC ratios were converted to standard deviation scores based again on the NHANES "normal" Caucasian population. Because the gender distribution of participants ≥ 40 years of age in the database (50.1% male) differed slightly from that for the population (45.9% male), the data for men and women were weighted so that the resulting estimates of prevalence better represent the population. Additional weighting class adjustments [20] were made to adjust for differential response rates for the eight categories defined by gender and age (*i.e.*, 40 to 49, 50 to 59, 60 to 69, and 70+ years).

The distributions of the main known risk factors available in the data set were also set out by age group and sex. These included family history of respiratory disease, education level, cigarettes smoking, water pipe (hookah) smoking, use of kangris and a history of tuberculosis.

Finally the standard deviation scores of the FEV1/FVC ratio were regressed against the main risk factors. These models included age, use of kangris, smoking of cigarettes and hookahs and the length of exposure to each of these in different combinations. All models adjusted for a family history of respiratory disease, educational level and exposure to passive smoking. Analyses were weighted using the survey commands in Stata. Regression diagnostics were done to check the assumption of normality of the error, homogeneity of the variance, and linearity between standardized score and predictors in the model.

Ethics

The study was approved by the Institutional Ethical Committee of the Sher-i-Kashmir Institute of Medical Sciences, Srinagar.

Results:

Of 1097 participants approached 41 provided no information and all we know of them is their age and sex. A further 103 (9%) provided information on smoking and diagnoses but did not provide further information, leaving 953 responders. The baseline characteristics of the responders and the non-responders are presented in table 1. Compared with the non-responders, the responders were more likely to be male (54% vs 36%, $p<0.001$), younger (54% vs 42% under 50 years old, $p<0.001$) and to have never smoked (46% vs 57%, $p<0.001$), but there was no significant difference in the prevalence of doctor diagnosed emphysema, COPD, asthma or chronic bronchitis (2% vs 3% , $p=0.8$) or of reported co-morbid conditions (27% vs 25%, $p=0.7$). Of the 953 responders, 757 (79%) provided adequate post-bronchodilator spirometry. Those with adequate spirometry were similar to those without except that they were more likely to have ever smoked cigarettes (13% vs 6%), though they had a similar overall exposure to tobacco of any type (55% vs 51%) and kangris each day (8 hours vs 8.13 hours).

Table 2 shows selected characteristics of the sample by sex. The women are shorter and spend much longer cooking with wood each day (3.7 vs 0.1 hours). They are also significantly more likely to have had no education (88% vs 65%) and are twice as likely to be overweight or obese (28% vs 14%). History of smoking (current or former) was higher among men (80.4%) compared to women (33%). Hookah smoking was more common among men than women at all ages. In the youngest age group smoking was less common in men under the age of 50 and in women under the age of 60, but cigarette smoking was more common among men under the age of 50 and was almost unreported by women. (Fig. S1).

Of the total population 16.1% had a FEV_1/FVC ratio below the lower limit of normal. (Table 3) This figure rose from 8.2% in those aged 40-49 years to 34.4 % in those over the age of 69 years and was higher in men (17.3%) than women (14.8%). Those who in addition had a FEV_1 <80% predicted for age, sex and height (modified stage II) were almost as numerous, 14.2% overall, 15.6% in men, 12.7% in women, 7.2% in those under 50 years old and 29.5% in those over the age of 69 years. The decline with age is greater than expected from the normal values given by the NHANES standard measures, and this is confirmed by the increasing prevalence of a value below the lower limit of normal as age progresses. The prevalence of obstruction, the proportion who are below the lower limit of normal, is 11.2% of men and 9.5% of women.

The prevalence of CAL was as high in the never smokers as among the general population, the group with the lowest prevalence being those smoking less than 10 pack-years. Among the never smokers the prevalence of CAL was marginally lower among women than among men. The prevalence of a self-reported doctor's diagnosis of COPD was 8.4/1000 and very much lower than the spirometrically diagnosed prevalence of chronic airflow obstruction.

Table 4 shows that the main risk factors are also strongly associated with age and these include length of exposure to cigarette smoking, hookah smoking and use of kangris. The main source of exposure to tobacco is from hookahs and these, unlike cigarettes, are commonly used by women as well as men. A reported family history of respiratory disease is not uncommon and is high in the youngest age group. A history of tuberculosis is rare. The great majority of the population is underweight by Western standards and very few are overweight or obese.

Table 5 shows the regression coefficients for standardised deviation score of FEV1/FVC. Visual checks of the diagnostic plots looked reasonable and indicated a good fit of the model. The first column (Unadjusted Model) gives the univariate associations which show significant negative associations with a family history of respiratory disease, age, use of kangris, use of hookahs and farming and positive associations with higher education. Mutual adjustment for family history, education, age and passive smoke exposure (Model 1) shows that all these variables have independent effects. Removing age from the model but adding years of hookah use and years of kangri use (Model 2) shows significant associations for both of these exposures. Adjusting for age again (Model 3) shows no significant association with age but removes the significance of the effect of kangri use, even though the coefficient is unchanged. The effect of hookah use remained significant. BMI is not associated with the outcome in the unadjusted comparison and this is true also for the final adjusted models. Exposure to passive smoking is negatively, but not significantly, associated with the FEV1/FVC ratio in the unadjusted model. When the final model is adjusted for passive smoking most of the associations are strengthened but the association with passive smoking is reversed and is only of borderline significance.

Whichever model is examined there are significant independent associations with a family history of respiratory disease, education, and hookah smoking. Kangri use is only significant if age is left out of the model and if age and kangri use are included in the model neither kangri use nor age are significantly associated with the FEV1/FVC ratio. The adverse association with passive smoking seen in the model adjusted simply for age, family history and education is reversed in the more fully adjusted models.

The association of the FEV1/FVC ratio to selected risk factors may be expressed as both a continuous measure of FEV1/FVC and as the prevalence of those with a ratio less than the lower limit of normal. Smoking is not associated with a low FEV1/FVC ratio in this study though the former-smokers tend to have the worst ratios. . The highest prevalence of obstruction is in the small number who smoked at least 20 pack years, but as there were only 12 of these the analysis has little power to show an effect. There is a tendency for those exposed to passive smoke to be at higher risk. Longer hours cooking with wood and biomass were associated with worse lung function, though this was only clearly significant for the analysis of the binary variable. Lack of education also appeared to be a risk factor, though this was only significant for the analysis of the continuous variable.

Discussion:

Our results show that about a sixth of the population aged $\geq$ 40 years in Kashmir has Stage I or higher CAL but that only 0.73% report doctor-diagnosed COPD. These figures show a much higher burden of CAL in our population compared to previous national estimates,[12] but a previous questionnaire and peak flow meter based survey reported a prevalence of chronic bronchitis in Kashmir to be 7.7%, with higher prevalence among smokers and those living in poorly-ventilated houses. [21] The prevalence of CAL in our population is much higher than other comparable low income centres in India such as Pune and Mumbai.[11]

The single most important cause of airflow obstruction was smoking and smoking prevalence was high, particularly smoking of traditional hookahs among the older population. Whereas the use of hookahs was widespread among both men and women, cigarette smoking was confined to the younger men. We have earlier reported hookah smoking to confer a higher risk of lung cancer compared to cigarette smoking, [22] and the current study shows that it may be an important contributory factor in the causation of CAL as well. In Kashmiri hookahs molasses is added to the tobacco with direct contact beween the live charcoal embers and the tobacco in the head of the hookah. This leads to higher temperatures as compared to other Shishas where a metal foil separates the tobacco from burning charcoal. This unique feature may subject the tobacco to greater pyrolysis and result in a higher concentration of the products of combustion of tobacco as well as the burning wood charcoal. In addition, the water in the body of the hookah may not be changed for many days which could lead to a higher concentration of the toxic products in the water through which the smoke passes prior to inhalation.[23]

Kashmir is a moderate altitude area with severe winters that confine people to homes for prolonged periods with potentially higher exposures to indoor air pollution by way of much more use of biomass fuel for heating and cooking. Kangris are used for personal heating which provide a very close exposure to biomass fuel. Although it has been argued that the use of indoor biomass fuels may explain the high mortality rates from COPD in low income countries,[24] we were unable to show a convincing association between use of biomass and airflow obstruction. Although this could be due to a universally high exposure, the lack of a measurable effect is consistent with the results from an earlier BOLD analysis,[25] and from the Kedourie cohort.[26] We did find suggestive evidence of an association with greater exposure to kangris.

Exposure to passive smoking was negatively, but not significantly, associated with the obstruction before adjustment for potential confounders. However, when our final model was adjusted for passive smoking most of the associations were strengthened but the association with passive smoking was reversed and was only of borderline significance. All these exposures were too highly correlated with age and with each other to entirely distinguish the individual effects of each. In so far as these could be disentangled the most likely cause of the high prevalence of obstruction is the extensive use of hookah smoking.

We found a significant association of family history of respiratory disease and poor education with a high prevalence of CAL. Health outcomes consistently show significant social gradients and improving access to education is regarded as one of the major social interventions for addressing the huge burden of non-communicable diseases (NCD).[27] While our findings lend additional support to this view, a clear explanation for the association is still lacking.

Kashmiris are also ethnically and phenotypically different from the rest of India and a preliminary principal component analysis has suggested a genetic relation to Europeans.[28]

The highest burden of CAL in our study was in men $\geq$ 70 years and women $\geq$ 60 years. India has witnessed a change in the average life span from an average of 37 years in 1950 to about 69 years in 2010,[29] and further ageing of the population is going to be an important determinant of the prevalence of the disease in the country in future. Developing countries are experiencing an ever increasing burden of NCDs. In India NCDs account for 53% of all deaths and 44% of disability-adjusted life-years, and are projected to constitute 67% of total deaths by 2030.[30] Of these, chronic respiratory disease accounts for 7% deaths and 3% DALYs lost. [31] The number of COPD patients is projected to be 22 million by 2016, many requiring hospitalization, burdening the already resource-constrained healthcare system. [32] India contributes a significant and growing percentage of global COPD mortality.[33]

We used the lower limits of normal (LLN) of FEV1/FVC ratio for defining CAL as against the fixed ratio (recommended by GOLD) as the GOLD criterion does not take into account the decline in lung function with age [34] and is less able to identify related abnormalities. [35] As there is little evidence for any substantial difference in the FEV1/FVC ratio between ethnic groups,[13,33,36,37] we have used the equations from the NHANES study to estimate the LLN and the % predicted. The adequacy of this single standard is confirmed by an analysis substituting normal values generated from the Kashmir data which gave very similar answers.

A striking finding in this study was the wide gap between the estimates of doctor diagnosed COPD and that of the actual prevalence. Sensitization of medical personnel to the need for increased use of spirometry in diagnosing CAL is thus required. This should be undertaken in tandem with awareness activities to disseminate the preventable nature of CAL. The use of bronchodilators or inhaled corticosteroids was also low in tandem with other Low and Middle Income countries. The estimated rate of usage of a inhaled bronchodilator/inhaled corticosteroid being 2.4% whereas that of influenza vaccine was nil,[38] dictated by a number of factors including local beliefs and misperceptions regarding the use of inhalational devices.[39]

Our study is limited by the fact that the largely rural setting of the study area may not be representative of the whole country where occupations, patterns of usage of biomass fuel or other socio-cultural practices differ. However the strengths of the study are its robust design, the objective evidence of airflow limitation and the homogeneity of the population studied. Since participants with acceptable spiromtery constituted <80% of the recruited, there is a possibility of some bias. However, it is likely to be small in an association study with a response rate of around 70% in which the major confounders (age, gender and smoking) have been adjusted for and where the weighting has been employed to take account of age-sex distribution of the original population.

In conclusion CAL is highly prevalent in Kashmir and similar studies need to be undertaken across the country to get an accurate assessment of the burden of COPD in the ever increasing and ageing population of the second most populous country in the world. Interventions aimed at prevention and cessation of smoking including the use of hookahs is essential to prevent the impending explosion of tobacco-related diseases including COPD, cancer and cardiovascular disease. The use of biomass fuels and in particular the use of kangris and their possible role in causing chronic lung disease requires further evaluation.

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Table 1. Comparison of responders and non-responders

		Responders[1]	Non-responders[2]	P-value[5]	Responder[3]	Non-responder[4]	
Age		N = 953	N=144		N=757	N=340	p-Value[5]
	40-49	515 (54%)	60 (42%)		423 (56%)	147 (45%)	
	50-59	215 (23%)	23 (16%)		158 (21%)	77 (24%)	
	60-69	147 (15%)	34 (23%)		118 (16%)	58 (18%)	
	70+	76 (8%)	27 (19%)	<0.001	58 (8%)	44 (14%)	0.002
Gender		N=953	N=144		414 (55%)	142 (44%)	
	Male	510 (54%)	52 (36%)	<0.001	343 (45%)	184 (56%)	<0.001
	Female	443 (46%)	92 (64%)				
Smoking status[6]		N=953	N=103		357 (47%)	88 (30%)	
	Current	445 (47%)	1 (1%)	<0.001	59 (8%)	54 (18%)	
	Ex	70 (7%)	43 (42%)		341 (45%)	154 (52%)	<0.001
	Never	438 (46%)	59 (57%)				
Doctor diagnosed asthma, emphysema, CB or COPD		N=953	N=103		19 (3%)	7 (2%)	
	Yes	23 (2%)	3 (3%)	0.756	738 (97%)	289 (98%)	<0.001
	No	930 (98%)	100 (97%)				
Other co-morbid conditions		N=953	N=103		214 (28%)	72 (24%)	
	Yes	260 (27%)	26 (25%)	0.658	543 (72%)	224 (76%)	0.196
	No	693 (73%)	77 (75%)				

1. Responders are those who completed post-BD spirometry (regardless of QC scores) and the core questionnaire.
2. Non-responders are eligible individuals who are missing the core questionnaire and/or post-BD spirometry, but for whom the tabulated variable is known.
3. Responders with acceptable spirometry
4. Non-responder in 2 and responder with non-acceptable spirometry
5. Two-sided p-value based on Pearson chi-square test.
6. Smoking status by any tobacco smoking

Table 2: Characteristics of the sample according to sex

			Male	Female	p
N			510	443	
Age	Years	Mean (s.d.)	52(10.53)	51.24(10.04)	0.26
Height	cms	Mean (s.d.)	165.64(6.65)	154.02(6.82)	<0.001
FVC	L	Mean (s.d.)	3.75 (0.74)	2.66(0.03)	<0.001
FEV1/FVC (%)		Mean (s.d.)	75.15(11.23)	77.91(9.57)	<0.001
Predicted FEV1/FVC (%)		Mean (s.d.)	77.42 (2.16)	79.94 (2.19)	<0.001
Mean FEV1/FVC / Predicted		Mean (s.d.)	0.970 (0.13)	0.974 (0.11)	0.63
Fuel use	Cooking with Kerosene	N (%)	195(38.24)	161(36.34)	0.55
	Use of Kangri/hr/day	Mean (s.d.)	8(1.68)	8.13(1.08)	0.16
	Cooking with wood/hr/day	Mean (s.d.)	0.10(0.75)	3.69(1.29)	<0.001
Passive Smoking		N (%)	312(61.18)	308(69.53)	0.01
History of TB		N (%)	2(0.39)	3(0.68)	0.55
Doctor diagnosed COPD*		N (%)	4 (0.78)	4 (0.90)	0.53
Education	None	N (%)	329(64.76)	391(88.46)	<0.001
	Middle School	N (%)	82(16.14)	30(6.79)	
	High School	N (%)	77(15.16)	15(3.39)	
	Higher Education	N (%)	20(3.94)	6(1.36)	
BMI	Underweight	N (%)	57(11.18)	43(9.73)	<0.001
	Normal	N (%)	382(74.90)	275(62.22)	
	Overweight	N (%)	66(12.94)	89(20.14)	
	Obese	N (%)	5(0.98)	35(7.92)	
Smoking (Any)	Never	N (%)	138(25)	359(71)	<0.001
	Ex	N (%)	76(14)	37 (7)	
	Current	N (%)	337(61)	109(22)	
	/10 pack years	Mean (s.d.)	0.21(0.59)	0.002(0.04)	<0.001

* Which includes chronic bronchitis or emphysema

Table 3: Distribution of FEV1/FVC ratio and airway obstruction by age and sex

Sex	Age Group	N	FEV1/FVC	FEV1/FVC<LLN	FEV1/FVC<0.70
			Mean (SD)	% (SE)	% (SE)
Men	40-49	230	79.42 (8.06)	8.2 (3.0)	10.4(3.1)
	50-59	84	73.55 (10.33)	22.4 (6.6)	29.5(7.0)
	60-69	67	68.41 (12.33)	28.2 (5.8)	41.7(7.5)
	70+	33	63.12 (13.81)	45.9 (9.0)	66.6(2.3)
	Total	414	75.14 (11.21)	17.3 (4.5)	23.7(5.5)
Women	40-49	193	81.29 (7.40)	8.2 (3.0)	5.5(1.9)
	50-59	74	74.29 (11.55)	20.3 (4.8)	20.3(4.8)
	60-69	51	73.71 (8.21)	29.1 (8.7)	30.9(8.8)
	70+	25	71.16 (10.41)	21.8 (6.9)	33.8(12.6)
	Total	343	77.92 (9.54)	14.8 (2.1)	14.5(2.1)
Population	40-49	423	80.27 (7.82)	8.2 (1.8)	8.0(1.7)
	50-59	158	73.89 (10.89)	21.4 (4.1)	25.0(4.2)
	60-69	118	70.70 (11.03)	28.6 (5.1)	36.8(5.9)
	70+	58	66.59 (12.90)	34.4 (6.4)	51.1(7.5)
	Total	757	76.40 (10.60)	16.1 (2.5)	19.3(2.9)

Table 4 Distribution of principal exposures by age and sex

Exposure	Sex	Men		Women	
	Age group	40-59	60+	40-59	60+
	N	383	127	347	96
Tobacco exposure					
Any tobacco smoking	Ever (%)	72	86	23	43
	Current (%)	65	67	19	7
	Pack years (mean, SD)	195 (169)	415 (290)	165 (150)	317 (217)
Cigarette smoking	Ever (%)	26	6	0.1	*
	Current (%)	22	3	0.1	*
	Pack years (mean, SD)	9.45 (7.48)	23.20 (18.16)	8.4	*
Sisha smoking	Ever (%)	59	84	23	43
	Current (%)	53	66	19	37
	Pack years (mean, SD)	232 (161)	420 (289)	165 (150)	317 (217)
Passive smoking(exposed)	Current (%)	73	27	77	23
Exposure to Dusty job(Farming)					
Farming	Ever (%)	61	39	63	37
Years in Farming	Exposure (mean, SD)	27.26 (9.61)	46.43 (9.85)	25.49 (7.07)	40 (9.32)
Indoor Air Pollution Exposure					
Wood for cooking	Ever (%)	75	25	78	22

Years exposed	Exposure (mean, SD)	40.50 (6.09)	60.97 (5.71)	39.75 (7.09)	58.44 (6.94)
Wood for heating	Ever (%)	75	25	78	22
Years exposed	Exposure (mean, SD)	40.00 (6.95)	60.57 (6.29)	39.15 (7.93)	58.35 (6.87)
Use of Kangri	Ever (%)	75	25	78	22
Years exposed	Exposure (mean, SD)	37.09 (6.03)	57.51 (5.21)	36.87 (5.94)	56.77 (6.41)
Education					
Education	None (%)	57	87	86	98
	Primary (%)	20	5	8	1
	Higher (%)	22	9	6	1
Body Mass Index					
Body Mass Index	Underweight (%)	75	75	63	58
	Normal (%)	10	14	9	13
	Overweight	14	10	21	19
	Obese	1	1	7	10
Family History of Respiratory diseases					
Family history	Yes (%)	67	33	91	10
History of Tuberculosis					
TB History	Positive (%)	0.3	0.8	0.9	0

*: No observation

Table 5 Different models for the associations of risk factors with the standardised score of the FEV1/FVC ratio

	Univariate Regression			Model 1			Model 2			Model 3		
R-square				0.1049			0.1373			0.1372		
	Coefficient	95% CI	(p)	Coefficient	95% CI	(p)	Coefficient	95% CI	(p)	Coefficient	95% CI	(p)
Family History of Resp Dis	-0.962	(-1.86,-0.07)	0.04	-1.063	(-0.06,-0.02)	0.01	-0.989	(-1.69,-0.29)	0.01	-0.992	(-1.67,-0.29)	0.01
Education: none	*Reference*			*Reference*			*Reference*			*Reference*		
Education: primary	0.661	(0.09,1.23)	<0.001	0.412	(-0.16,0.99)	<0.001	0.453	(-0.14,1.04)	0.04	0.452	(-0.13,1.04)	0.04
Education: higher	0.731	(0.45,1.01)		0.439	(0.25,0.63)		0.373	(0.12,0.62)		0.372	(0.12,0.62)	
Age/year	-0.045	(-0.07,-0.02)	<0.001	-0.04	(-0.61,-0.02)	<0.001				-0.004	(-0.05,0.04)	0.83
Exposure to kangeri/year	-0.045	(-0.07,-0.02)	<0.002				-0.030	(-0.05,-0.02)	<0.001	-0.027	(-0.07,0.02)	0.23
Use of water pipe	-0.756	(-1.27,-0.24)	0.01				-0.241	(-0.74,0.26)	0.30	-0.242	(-0.74,0.25)	0.29
Exposure to Farming	-0.019	(-0.03,0.00)	0.05									
Water pipe (pack years)	-0.002	(-0.003,-0.00)	0.01				-0.001	(-0.002,-0.0001)	0.03	-0.001	(-0.001,-0.0001)	0.03
Use of Cigarette	0.137	(-0.30,0.58)	0.49				-0.147	(-0.96,0.67)	0.69	-0.148	(-0.97,0.67)	0.69
Cigarettes (pack years)	-0.002	(-0.02,0.01)	0.71				-0.008	(-0.05,0.04)	0.67	-0.009	(-0.05,0.04)	0.66
Passive smoking	-0.176	(-0.46,0.11)	0.19									
BMI : Underweight	0.33	(-0.45,1.10)										
Normal	*Reference*		0.72									
Overweight	0.46	(-0.66,1.59)										
Obsess	0.21	(-1.72,1.51)										

Note: The SDS score is based on the standardized scores taken from the Caucasian sample of the National Health and Nutrition Examination Survey for the FEV1/FVC ratio Multivariate regression Model 1: Family history, education. Multivariate regression Model 2: Model 1 + exposure to Kangeri, smoking, use of water pipe, use of cigarettes, pack years of cigarettes, pack years of water pipe, passive smoking. Multivariate regression Model 3 : Model 2 + age