

Risk factors for Chronic Obstructive Pulmonary Disease in Non Smokers

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ABSTRACT

Background : Chronic obstructive airway disease (COPD) is one of the leading cause of morbidity and mortality worldwide. Apart from smoking, a known risk factor emerging evidence suggests that COPD is also prevalent in non smokers. Air pollution, occupational exposure and chemical exposure are suppose to be factors responsible for COPD in non smokers. Indoor air pollution is the most common risk factor for COPD in developing countries especially prevalent in females and rural population. This study was undertaken to find out frequency distribution of non smokers in COPD and to find out prevalence of risk factors in non smokers.

Material and Methods : This hospital based, observational case control study included 150 cases of COPD (65.3 %) smokers and (34.6 %) non smokers and 52 age sex matched healthy controls. Subjects were enroled after taking written consent. COPD was diagnosed on the basis of GOLD criteria. Subjects of COPD with severe comorbid conditions, passive smokers or in whom spirometry cannot be performed and those who are not willing to participate were excluded from the study. All cases underwent detailed clinical evaluation for risk factor profile and clinical manifestations BODE index was calculated.

Results : Frequency of non smokers in COPD was found to be 34.6%. In the cases of COPD non smokers group. Statistically significant difference was found in gender distribution. Indoor air pollution was the commonest risk factor reported in Non Smoker group. Exposure index in non smoker group was high as compared to controls. This difference was statistically significant. Exposure to cotton dust was another statistically significant risk factor found in nonsmoker group as compared to controls. Prior history of pulmonary tuberculosis was noted in 32.7% non smoker COPD as compared to 23.1% in controls. Multiple Logistic analysis demonstrated that, the indoor air pollution, weavers and history of pulmonary Koch's were statistically significant and independently associated with risk of COPD.

Conclusions : Substantial proportion of cases of COPD are non smokers. Indoor air pollution, prior history of pulmonary tuberculosis and occupational 9 cotton dust exposure are the prevalent risk factors in non smokers with COPD. Exposure to indoor pollution is the most prevalent risk factor in cases of non smokers associated with COPD.

Key words : Non-smoker COPD, BODE index, Indoor air pollutants.

Introduction :

Chronic obstructive pulmonary disease (COPD) is currently estimated to be the third cause of death globally¹ and is associated with reduction in quality of life for those affected² as well as economic burden to society³. As the association between smoking and COPD is so strong, it has often been seen as a smoker's disease. However, emerging evidence suggests that other risk factors, viz. indoor air pollution (biomass fuel, wood and coal), occupational exposures (crop and animal farming, dust exposure - coal, gold and iron, steel founding),

chemical exposures (plastic, textile, rubber and leather) and outdoor air pollution are important especially in developing countries. COPD is also reported to be associated with chronic asthma, past history of tuberculosis, childhood respiratory infections, poor socio-economic status, and poor nutrition. Occupational exposure to noxious substances, such as vapours, gas, dust and fumes has been implicated as a cause of COPD in approximately 15% of cases several occupational categories, such as mining workers, farmers and construction workers, have been associated with an increased risk of COPD⁴. Importantly, in several studies never-smokers consistently constitute a considerable proportion of all subjects with COPD, ranging from 25-45%^{4,5}. To what extent COPD among never-smokers presents with a different clinical profile than that of smokers with COPD has yet to be determined. From population-

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based surveys we know that very severe degree of airflow limitation is less commonly found in never-smokers with COPD as compared to smokers with COPD⁶.

Methodology :

This hospital based, observational cross sectional study was initiated after getting approval from Institutes' Ethics Committee. 150 cases of COPD (smokers and non smokers) attending Medicine out patient clinic with age >21 years and willing to participate in the study were included after obtaining written informed consent. COPD was diagnosed on the basis of spirometry demonstrating post bronchodilator FEV1 / FVC <0.7. Cases of COPD with acute exacerbation or serious comorbid conditions, passive smokers, patients with active tuberculosis, Ischaemic heart disease, restrictive heart disease and those in whom spirometry cannot be performed, were excluded from the study. 52 age and gender matched healthy controls were included in the study. All cases underwent detailed clinical evaluation for the presence of risk factors, clinical profile, severity assessment as per the GOLD criteria and BODE index was calculated. Risk factors other than smoking viz .indoor air pollution (biomass fuel, wood and coal), occupational exposures (crop and animal farming), dust exposure (coal, gold and iron, steel founding), chemical exposures (plastic, textile, rubber and leather and outdoor air pollution) were assessed .

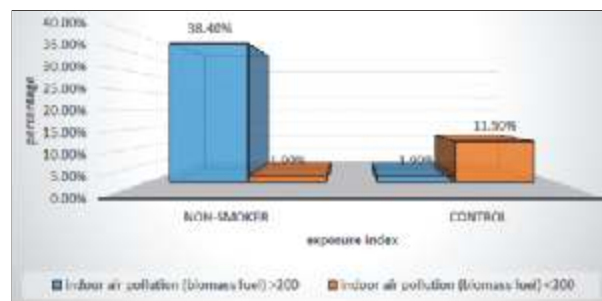
Results :

Study included total 150 cases of COPD out of which 98 (65.3%) were smokers and 52 (34.6%) were non smokers. Mean age in COPD smokers group was 59.31 ± 8.7 . Mean age of all cases of COPD was 60.15 ± 7.9 years (p 0.2NS).

In the non smokers group, 29 (55.8%) were females and 23 (44.2%) were males in smokers group all 98 (100%) cases were males demonstrating significant gender distribution (p<0.001) In total 150 cases of COPD, 121 (80.7%) were males & 29 (19.3%) were females.

Indoor air pollution was the commonest risk factor reported in 21 (40.4%) cases of COPD in Non Smoker group and (7, 13.5%) controls and the difference was statistically significant (OR 4.35, 95% CI 1.65 -11.4, p<0.004).

Fig. 1 : Exposure index of indoor air pollution in non smokers COPD and controls



Exposure to cotton dust (Weavers) as the occupational risk factor as compared to controls revealed statistically significant difference.

Prior history of pulmonary tuberculosis and working in the transportation / trucking and automobile repairs was not found to be significantly associated with Non smoker COPD as compared to controls. Industrial exposure was found in few of non smoker COPD group but none of the controls had such history. Working in the farm and exposure to livestock, low socio-economic status and age of the person were also not found to be significantly associated with COPD in non smoker group as compared to controls. Interestingly residing in rural area was found to be statistically significant in non smoker COPD as compared to controls.

Multiple Logistic Analysis was performed with presence or absence of COPD as dichotomous dependent outcome variable with risk factors of COPD (other than smoking in non-smokers and controls) as independent predictor variables, in order to determine the independent association of COPD with risk factors. **In this model indoor air pollution (biomass fuel), occupational exposure (weaver), resident, and History of pulmonary Koch's are taken as categorical variables. The analysis shows that after multiple logistic regression, the indoor air pollution, weavers (occupational exposure), and history of pulmonary Koch's were statistically significant and independently associated with risk of COPD.**

Risk factors other than smoking in smokers and non smokers

Indoor air pollution (biomass fuel exposure) as a risk factor was seen statistically significant in non smoker COPD as compared to smoker COPD. 20

Table 1 : Association of risk factors in non smokers COPD and controls

Risk Factors	Non Smokers (n = 52)	Controls (n = 52)	p-value, chi sq. odds ratio (95% CI)
a) Indoor air pollution (biomass fuel) (n = 28)	21 (40.4%)	7 (13.5%)	OR = 4.355 95% CI 1.651 - 11.488 $\text{CHI}^2 = 9.579$ p = 0.004 HS
b) History of Pulmonary Koch's (n = 29)	17 (32.7%)	12 (23.1%)	OR = 1.619 95% CI 0.68 - 3.853 $\text{CHI}^2 = 1.145$ p = 0.382 NS
c) Occupational exposure 1. Weaver (n = 11)	10 (19.2%)	01 (1.9%)	OR = 12.143 95% CI 1.443 - 8.754 $\text{CHI}^2 = 8.235$ p = 0.008 HS
2. Transportation/ Trucking Or automobile repair (n = 3)	02 (3.8%)	01 (1.9%)	OR = 2.040 95% CI 0.179 - 23.217 $\text{CHI}^2 = 0.343$ p = 1.000 NS
3. Industrial worker (n = 2)	02 (3.8%)	00 (0.0%)	OR = 0.490 95% CI 0.402 - 0.593 $\text{CHI}^2 = 2.039$ p = 0.495 NS
d) Farming /Livestock Workers (n = 8)	03 (5.8%)	05 (9.6%)	OR = 0.576 95% CI 0.130 - 2.544 $\text{CHI}^2 = 0.542$ p = 0.175 NS
e) Socio-economic status (kuppuswami scale)			$\text{CHI}^2 = 1.533$ p = 0.465 NS
lower (n = 16)	06 (11.5%)	10 (19.2%)	
lower middle (n = 58)	29 (55.8%)	29 (55.8%)	
upper (n = 30)	17 (32.7%)	13 (25%)	
f) Age (≥ 65) (n = 44)	24 (46.2%)	20 (38.5%)	OR = 1.371 95% CI 0.628 - 2.993 $\text{CHI}^2 = 0.630$ p = 0.552 NS

Table 2 : Showing Multiple Logistic Analysis

Risk Factors	Adjusted OR	95% CI	Pvalue
Indoor air pollution (biomass fuel)	13.420	3.095 - 58.185	p = 0.0005 HS
Weaver	85.112	8.406 - 861.70	p = 0.0002 HS
Area of living (resident)	2.9149	0.907 - 9.3617	p = 0.0723 NS
History of Pulmonary Koch's	9.850	2.690 - 35.95	p = 0.0002 HS

(38.4%) cases of non smokers COPD had Exposure index for indoor air pollution (biomass fuel) >200 while in none of the case from smokers COPD had exposure index >200 ($p < 0.01S$.)

Prior history of pulmonary Koch's, Occupational exposure to Cotton dust (weavers) and low socio-economic status were found to have statistically significant association between non smokers COPD as compared to smoker COPD. On the contrary risk factors like occupation as

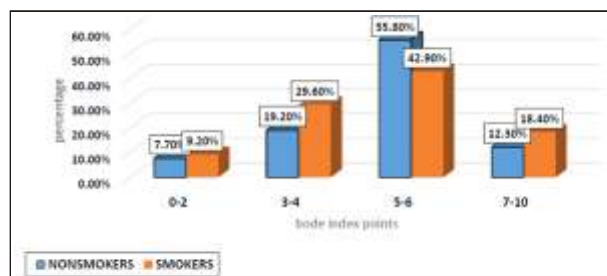
transportation / trucking and automobile repairs, farming / livestock worker and history of working in industries were not associated significantly in non smoker COPD as compared to smoker COPD cases of smokers with COPD.

24 (46.1%) cases from non smokers COPD and 11 (11.2 %) from smokers with COPD were living in rural areas and the difference was statistically significant. (OR 6.779 95% CI 2.952 - 15.563 p, 0.0001 HS).

Table 3 : Association of risk factors of COPD in non-smokers and smokers COPD other than smoking

Risk Factors	Non Smokers (n = 52)	Smokers (n = 98)	p-value, chi sq. odds ratio (95% CI)
a) Indoor air pollution (biomass fuel) (n = 23)	21 (40.4%)	02 (2%)	OR = 32.516 95% CI 7.21 - 146.5 $\text{CHI}^2 = 38.475$ p = 0.0001 HS
b) History of Pulmonary Koch's (n = 23)	17 (32.7%)	06 (6.1%)	OR = 0.134 95% CI 0.049 - 0.368 $\text{CHI}^2 = 18.474$ p = 0.0001 HS
c) Occupational exposure 1. Weaver (n = 10)	10 (19.2%)	00 (0.0%)	OR = 0.300 95% CI 0.233 - 0.386 $\text{CHI}^2 = 20.192$ p = 0.0001 HS
2. Transportation / Trucking Or automobile repair (n = 7)	02 (3.8%)	05 (5.1%)	OR = 1.344 95% CI 0.252 - 7.179 $\text{CHI}^2 = 0.120$ p = 1.000 NS
3. Industrial worker (n = 2)	02 (3.8%)	00 (0.0%)	OR = 0.338 95% CI 0.270 - 0.423 $\text{CHI}^2 = 3.820$ p = 0.119 NS
d) Farming / Livestock Workers (n = 7)	03 (5.8%)	04 (4.1%)	OR = 1.438 95% CI 0.309 - 6.68 $\text{CHI}^2 = 0.217$ p = 0.694 NS
e) Socio-economic status (kuppuswami scale)			$\text{CHI}^2 = 8.133$ p = 0.017 HS
lower (n = 23)	06 (11.5%)	17 (17.3%)	
lower middle (n = 97)	29 (55.8%)	68 (69.4%)	
upper (n = 30)	17 (32.7%)	13 (13.2%)	
f) Age (≥ 65 years) (n = 60)	24 (46.2%)	36 (36.7%)	OR = 1.476 95% CI 0.745 - 2.921 $\text{CHI}^2 = 1.256$ p = 0.296 NS

Pulmonary function tests, GOLD staging and BODE index did not differ significantly in smokers and non smoker COPD as shown in **Table 4**.

Fig. 2 : BODE index in COPD - smokers and non smokers**Discussion :**

Traditionally, it has been believed that tobacco smoking is the only major risk factor associated with development of COPD. Apart from tobacco smoking, however, emerging evidence suggests that other risk factors, viz. indoor air pollution (biomass fuel, wood and coal), occupational exposures (crop and animal farming, dust exposure coal, gold and iron, steel founding), chemical exposures (plastic, textile, rubber and leather) and outdoor air pollution are important especially in developing countries. Present study demonstrated high prevalence (34.6%) of non smokers in cases of COPD. Salvi *et al* 4 found prevalence of non smokers in COPD to be 25-45% and **Lamprecht *et al*** 7 found 36.9%

Table 4 : Comparison of mean PFT findings in cases-non smokers COPD and smoker COPD

Gold staging	Non Smokers (n = 52)	Smokers (n = 98)	Total (n = 150)	p-value, chi sq. Odds ratio (95% CI)
Mild (n = 13)	04 (7.7%)	09 (9.2%)	13 (8.7%)	OR = 0.824 95% CI 0.241 - 2.816 CHI ² = 0.095 p = 1.000 NS
Moderate (n = 71)	28 (53.8%)	43 (43.9%)	71 (47.3%)	OR = 1.492 95% CI 0.759 - 2.932 CHI ² = 1.354 p = 0.321 NS
Severe (n = 48)	17 (32.7%)	31 (31.6%)	48 (32%)	OR = 1.049 95% CI 0.511 - 2.154 CHI ² = 0.0175 p = 1.000 NS
Very Severe (n = 13)	03 (5.8%)	11 (11.2%)	14 (9.3%)	OR = 0.484 95% CI 0.128 - 1.819 CHI ² = 1.194 p = 0.381 NS

Table 5 : Gold staging in cases of COPD - smokers and nonsmokers

Gold staging	Non Smokers (n = 52)	Smokers (n = 98)	Total (n = 150)	p-value, chi sq. Odds ratio (95% CI)
Mild (n = 13)	04 (7.7%)	09 (9.2%)	13 (8.7%)	OR = 0.824 95% CI 0.241 - 2.816 CHI ² = 0.095 p = 1.000 NS
Moderate (n = 71)	28 (53.8%)	43 (43.9%)	71 (47.3%)	OR = 1.492 95% CI 0.759 - 2.932 CHI ² = 1.354 p = 0.321 NS
Severe (n = 48)	17 (32.7%)	31 (31.6%)	48 (32%)	OR = 1.049 95% CI 0.511 - 2.154 CHI ² = 0.0175 p = 1.000 NS
Very Severe (n = 13)	03 (5.8%)	11 (11.2%)	14 (9.3%)	OR = 0.484 95% CI 0.128 - 1.819 CHI ² = 1.194 p = 0.381 NS

Various studies have already documented that overall prevalence of COPD in males is higher than females. **Davies adeloje *et al*⁸** in a study found that the overall prevalence in men aged 30 years or more was 14.3% (95% CI 13.3% - 15.3%) compared to 7.6% (95% CI 7.0% - 8.2%) in women. **However, COPD in non smokers affects females more commonly than males present study has a the**

ratio of female / male were 1.26, showing that COPD in non-smokers more common in females as compared to males, due to more percentage of female's exposure to biomass.⁹ **Jindal SK *et al*¹⁰** study found that the prevalence of COPD was more among females as compared to males in Non-smokers COPD. In the population-based **BOLD** study⁷, it was reported that never smokers made up

27.7% (523/1,889) of all COPD cases, and 70.8% of non-smokers with COPD were females.

Present Study revealed indoor air pollution (biomass fuel) as the commonest risk factor associated with COPD in non smokers 21 (40.4%) as compared to controls 7 (13.5%) (**p=0.004**) with **OR=4.355, 95% CI 1.651-11.488, CHI2=9.579. Cotton dust exposure was prevalent in 10 (19.2%) cases of COPD non smokers group and 1 (1.9%) of controls, demonstrating a statistically significant difference (OR=12.143, 95% CI 1.443-8.754, CHI2=8.235.) Prior history of pulmonary Koch's was also associated as a risk factor, present in 17 (32.7%) cases of non smokers COPD group and 12 (23.1%) Controls (OR=1.619 and 95% CI of 0.68-3.853 Multiple logistic regression analysis** was performed where COPD was taken as dependent dichotomous variable and risk factors other than smoking as independent variable in non-smokers COPD and controls, in which the **indoor air pollution (biomass fuel)** (p=0.0005), **occupational exposure (weavers)** (p=0.0002) and **History of pulmonary Koch's** (p=0.0005) was found to risk factors which are independently associated with risk of COPD.

Present study also demonstrated significant difference in exposure index (>200) for indoor air pollution - biomass fuel - reported in (38.4%) cases as compared to controls (1.9%, p0.0001) comparison of risk factors (other than smoking) in smokers and non smokers COPD group also demonstrated that Indoor air pollution (OR=32.516 95% CI 7.21-146.5 CHI2=38.475 **p=0.0001 HS0, history of pulmonary Koch's** (OR=0.134 95% CI 0.049-0.368 CHI2=18.474 **p=0.0001 HS)** and **occupational exposure (weaver, cotton dust)** (OR=0.300 95% CI 0.233-0.386 CHI2=20.192 **p=0.0001 HS)** and **low socioeconomic status** CHI2=8.133 **p=0.017 HS** Exposure to indoor air pollution (biomass fuel) was noted in, 21(40.4%) out of 52 COPD in **were significantly associated with COPD in non smokers.**

Globally, 3 billion individuals are estimated to use biomass fuel for heating or cooking purposes in the home. 135 several studies have confirmed exposure to biomass fuel as a risk factor for COPD. **HU G et al¹¹** study in 2010 observed that Overall, people

exposed to biomass smoke have an odds ratio (OR) of 2.44 (95% CI, 1.9-3.33) for developing COPD, relative to those not exposed to biomass smoke. Biomass smoke exposure was clearly identified as a risk factor for developing COPD in both women (OR, 2.73; 95% CI, 2.28-3.28) and men (OR, 4.30; 95% CI, 1.85-10.01), and in both the Asian population (OR, 2.31; 95% CI, 1.41-3.78) and the non-Asian population (OR, 2.56; 95% CI, 1.71-3.83). This risk factor has also been revealed in patients with chronic bronchitis (OR, 2.56; 95% CI, 1.77-3.70) and COPD (OR, 2.65; 95% CI, 1.75-4.03), and in cigarette smokers (OR, 4.39; 95% CI, 1.40-4.66) and non-cigarette smokers (OR, 2.55; 95% CI, 2.06- 3.15). **Camp PG et al¹²** in 2014 observed in this cross-sectional study, Women in the biomass group had significantly more air trapping than the tobacco group (radiologist score 2.6 and 1.5, respectively; p=0.02) and also scored lower on the symptom, activities and confidence domains of the quality of life assessment and had lower oxygen saturation at rest and during exercise (p<0.05).

Lindstrom et al¹³ reported that risk factors viz. Age, family history, indoor air pollution from biomass fuel, manual work are associated with COPD in never smoked subjects while Zhou et al¹⁴ in his study mentioned that Male sex, age, low educational attainment, low body-mass index, family history of respiratory disease, exposure to biomass for cooking, exposure to coal for heating, poor ventilation in kitchen, chronic cough in childhood are the significant risk factors for COPD in non smokers Ehrlich et al¹⁵ reported Domestic fuel, occupational exposure, history of pulmonary tuberculosis, female gender as the risk factors while Caballero et al¹⁶ found Age, male sex, history of tuberculosis, wood smoke exposure (=10 years), low educational attainment significantly associated with COPD.

As it is already evident and documented by various multicentric studies that COPD can affect non smokers and the various risk factors identified, and published by researchers, indoor air pollution has been emerged to be the commonest and most important risk factor, especially in the developing countries. The biomass fuel is used rampantly for cooking the duration and amount of exposure of the

biomass is reported to be high. Women especially in the rural areas, comprise the population at high risk to acquire COPD, affecting their quality of life, morbidity and mortality. Not only the women, children are at also high risk as they are exposed to biomass as they most of the times accompany their mothers while cooking getting heavily exposed to indoor air pollution. Pulmonary tuberculosis is prevalent in developing countries and is also documented to be a significant risk factor for COPD in non smokers. Weavers exposed to the cotton dust is also an important risk factor in our population as large no .of subjects are engaged in it. Salvi et al in his study has documented the high prevalence of COPD in non smokers, women, children and in previously treated cases of pulmonary tuberculosis ,asthma and those with childhood respiratory infections. Outdoor air pollution ,transportation and trucking, farming and livestock exposure are also the factors associated with COPD, exposure of which needs to be reduced, to prevent the development of COPD and to reduce morbidity and mortality associated with it and to improve quality of life in these individuals, large sample sized, population based studies are needed to document exact prevalence of risk factors especially in the rural region. Cases of COPD who are smokers may also have additional risk factors apart from smoking, however, whether these factors clinically influence severity and outcome, needs to be assessed in further studies.

Present study, however, did not demonstrate any significant difference in the clinical presentation, severity and short term outcomes in cases of COPD smokers and non smokers however, needs to be confirmed in large sample sized, prospective multicentric population studies

Conclusions :

Substantial proportion of cases of COPD are non smokers. Indoor air pollution, prior history of pulmonary tuberculosis and occupational 9 cotton dust exposure are the prevalent risk factors in non smokers with COPD. Exposure to indoor pollution is the most prevalent risk factor in cases of non smokers associated with COPD. COPD in non smokers is common in females as compared to males.

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