Occupational exposures and chronic obstructive pulmonary disease: a hospital based case–control study

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ABSTRACT

Background Occupational exposures are associated with chronic obstructive pulmonary disease (COPD). This study investigated this association among a population with a high prevalence of tuberculosis and smoking.

Methods Cases (n=110) diagnosed by pulmonologists were selected from specialist respiratory clinics. Frequency sex- and age-matched controls (n=102) were selected from other clinics at the same institutions. Lifetime occupational exposure histories were obtained through interviews. Exposure variables derived from the ALOHA Job Exposure Matrix (JEM) were used to complement the self-reporting variables. ORs were calculated from logistic regression models, adjusting for smoking and past history of tuberculosis. Percentage population attributable risk (PAR%) was also calculated.

Results The adjusted ORs for COPD from the JEM-derived high cumulative biological dust exposure, high cumulative mineral dust exposure and high cumulative gas and fumes exposure were 2.1 (95% CI 1.1 to 4.2), 1.1 (95% CI 0.6 to 2.4) and 1.8 (95% CI 0.8 to 3.9), respectively. Self-reported occupational exposures were associated with higher risks, with adjusted ORs for high dust exposure-years and high chemical, gas and fumes exposure-years of 5.9 (95% CI 2.6 to 13.2) and 3.6 (95% CI 1.6 to 7.9), respectively. Among ever smokers, there was an increased risk for COPD, with ORs ranging from 5.0 to 5.5. Tuberculosis was a strong risk factor, with an OR ranging from 7.7 to 8.1. The PAR% was 25% for self-reported high exposures, but lower when the JEM variables were used.

Conclusions Lifetime occupational exposures contribute to the risk of COPD, adjusted for smoking. These risks are present in populations with a high burden of tuberculosis, which is considered an important causative factor.

Key Messages

What is the key question?

- Are occupational exposures associated with chronic obstructive airways disease in a population with ahigh prevalence of tuberculosis?

What is the bottom line?

- Occupational exposures contribute to the risk of chronic obstructive pulmonary disease, adjusted for smoking. These risks are present in populations with a high burden of tuberculosis, which is considered an important causative factor.

Why read on?

- Although occupational exposures have been consistently documented to be associated with chronic obstructive pulmonary disease over the last several years, there is a limited understanding of these associations in countries with other important risk factors such as chronic pulmonary infections. This study investigates associations among a high tuberculosis prevalence population.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is increasing worldwide, in both developed and developing countries. According to the 2001 World Bank/WHO Global Burden of Disease report, COPD is the sixth leading cause of death in developing countries, responsible for 4.9% of deaths.[1] Despite smoking being the most important risk factor for this disease, accounting for >75% of cases of disease, occupational exposures, alone or in combination with smoking, are responsible for a substantial proportion of disease.[1–3] Work may have an interactive effect with tobacco smoke, resulting in greater severity of disease with greater disability or by accelerating the rate of loss of lung function among those with the disease.[4]

Since the seminal paper on chronic airflow limitation and occupational exposures by Margaret Becklake in 1989, the evidence for work-related COPD has grown substantially.[5] Occupational exposures such as to vapours, gases, dusts and fumes present an important risk factor for the development of the disease, by itself and through interaction with other risk factors. A US study of >10 000 adults concluded that COPD attributable to work was ~19% in the total population, and 31.1% among never smokers.[6] The American Thoracic Society's consensus statement suggests that between 10% and 20% of COPD is attributable to workplace exposures.[2] The epidemiological evidence supporting the role of occupational exposures (organic and inorganic dusts, metal fumes, chemical vapours) as risk factors has been published in population-based studies,[6–8] and also studies regarding working environments with specific exposures.[9–12]

In developing countries, in addition to smoking, COPD is associated with the high burden of infectious respiratory diseases, particularly tuberculosis (TB).[13–15] The role of occupational exposures against this background of infectious diseases has not been investigated previously. This study

was undertaken to determine whether lifetime workplace exposures are associated with COPD, after adjusting for smoking, in a hospital sample of patients with known COPD, compared with hospital-selected controls among a population with elevated prevalence of TB.

METHODS

Selection of clinics and participants

This hospital-based study was conducted at three tertiary public health hospitals in KwaZulu-Natal province of South Africa. Ethical approval was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, and participation was voluntary. The three specialist respiratory centres that exist in the province are located at these institutions. Cases of COPD were defined on the basis of a pulmonologist diagnosis. These specialists employed the Global Initiative on Obstructive Lung Disease (GOLD) definition using spirometric assessments.[16] All patients, presenting for the first time or for follow-up visits to these centres over a 6-month period, and meeting this case definition, irrespective of severity, age or current employment status, were invited to participate. Controls were drawn from clinics other than those for respiratory chronic diseases (the cardiovascular, renal and diabetes clinics) at the same institutions, selected over the same time period as the cases. Potential controls were excluded if they reported ever having had a diagnosis of COPD, asthma, chronic bronchitis or emphysema, or if they had used any COPD medication including inhalers within the past 12 months. No one was excluded on the basis of having had TB previously. This information was extracted from their hospital records, through consultation with the attending physician, and verified during the interview process. No chest radiographs or spirometry data were available for the controls. Controls and cases were group frequency matched for sex and age, within 5 years. One-to-one matching was not done. We were not able to obtain an equal number of control for all the cases that we had, despite several attempts. Participants were either English or isiZulu speakers.

Participant interviews

All participants were interviewed using instruments which had been translated into isiZulu, back-translated into English and extensively field tested in South Africa.[17] Interviews were conducted by trained interviewers in the language of choice (either English or isiZulu) of the participants. The questionnaire included questions on demographics, medical history, respiratory symptoms, smoking habits and family history, Another key covariate, TB, was assessed by asking 'have you ever had chest tuberculosis' (with a 'yes/no' response) and, if yes, 'was this confirmed by a doctor'.

Exposure assessment

Several questions concerning occupation were incorporated into the questionnaire, modified from the European Community Respiratory Health Survey (ECRHS) II.[18] These included: employment status, current and all previous jobs held (job description, industry, start and end date for each job), and self-reported occupational exposures for each job, up to a maximum of five. Information on all jobs held over the participant's working life (starting from current, and working towards since leaving school) was collected, up to a maximum of 10. If the employment was in the same industry but in different occupational categories, they were treated as different jobs. These latter series of questions were open ended. In addition, a series of closed questions relating to employment in industries with exposures associated with the development of COPD, including duration of exposure, were also included. These included questions on whether or not they had ever worked in a foundry, with asbestos, in a pottery, with diesel or diesel fumes, in a flax, cotton or hemp mill, in tunnelling, in drilling, in sandblasting, in a quarry and with any other dusty occupations or with chemicals. If a positive response was received for the latter industries, then the respondent had to indicate the duration of employment in that industry. The latter closed questions were used to validate the responses for the open-ended questions. The study region in South Africa is away from the major mining centres, and hence there was minimal mining exposure in our sample.

These jobs were then coded using the four-digit code of the International Standard Classification of Occupations (ISCO-88).[19] Using these codes, the ALOHA Job Exposure Matrix (JEM), previously used for COPD,[7 20] classified participants as having exposure to biological dusts, mineral dusts, gases and fumes. The ALOHA JEM scores 0, 1 and 2 (non, low, high) were squared before multiplying by duration. By summing the JEM-derived scores for years worked in these exposures, a cumulative exposure variable for each of these three exposure categories was established.

Statistical analysis

Data were analysed using STATA version 10.

Two composite exposure variables (dust, and chemicals, gases and fumes (CGF)) and duration of exposure to each were calculated from the self-reported data. The information from the open-ended questions reported by participants during the interview was used for analysis. For the logistic regression models, the exposure variables obtained through self-reporting and the JEM were used. Using exposed controls as the reference group, three exposure categories for each of these variables were obtained: non-exposed, low exposure and high exposure, using the median exposure among exposed controls as a cut-off point. Covariates of interest for COPD that were included in our logistic regression modelling included age, sex, smoking status and reported history of previous TB as confirmed by a doctor. All participants in the study were drawn from public sector hospitals, and therefore belonged to a narrow socio-economic stratum. For this reason, no adjustments for socio-economic status were done in the analysis.

Three logistic regression models were run, one for each exposure variable obtained through the JEM, and a further two models for each of the self-reported exposure history (to dust and CGF) were run. Smoking variables, categorised as never and ever smoking, evaluated the effect of smoking on risk of COPD. For the multivariate logistic regression models, ORs and 95% CIs are presented.

To determine the proportion of COPD cases attributable to occupational exposures, the percentage population attributable risk (PAR%) was calculated, using the method described by Weinmann *et al* ($PAR\% = ((OR-1)/(OR)) \times P_e$ where P_e=proportion of cases exposed). The ORs were those obtained from the logistic regression models.[21]

RESULTS

The sample comprised a total of 110 cases with a physician-confirmed diagnosis of COPD and 102 controls (table 1). According to the GOLD classification of COPD severity, 69.4% of cases were in stages III and IV, while none was in stage I. Of those invited to participate, three (two cases and one control)

Table 1 Demographic and smoking characteristics of cases and controls

Characteristic	Cases (n=110)	Controls (n=102)
Age (mean) (SD)		
Male	61.4 (9)	62.6 (8)
Female	62.5 (9)	58.5 (11)
Sex, n (%)		
Male	96 (87)	91 (89)
Female	14 (13)	11 (11)
Smoking status, n (%)		
Non-smokers	8 (7)	27 (26)
Ex-smokers	79 (72)	47 (46)
Current smokers	23 (21)	28 (27)
TB status		
History of TB	17 (15)	2 (2)

TB, tuberculosis.

refused. In both the groups, males constituted just fewer than 90% of participants. Cigarette smoking differed between cases and controls (93% vs 74% ever smokers); however, cases were more likely to be ex-smokers. Reported history of TB was greater among cases than controls (table 1).

The 110 cases reported a total of 340 job descriptions, compared with the 221 job descriptions reported by controls. A larger proportion of the controls reported employment in administrative (21% vs 12%), managerial (8% vs 3%) and quality control (5% vs 0.3%) positions compared with cases. Cases were more likely to be machinists (9% vs 6%), builders (8% vs 3 %) and fitters and turners (6% vs 2%) compared with controls (table 2).

All cases reported having at least one job over their lifetime, while among the controls 97% had at least one job over their lifetime, with 4 (4%) listing their jobs as full-time house persons. Employment status ('ever being employed') did not differ significantly between cases and controls. However, cases were more likely to be currently unemployed due to poor health than controls (53% vs 17%, $p<0.02$) (table 3).

Occupational exposures, measured through self-reporting and JEM, were more common among the cases than controls. Self-reported exposure to dust, CGF and mixed dust–CGF exposure was significantly different between cases and controls (table 3).

The duration of self-reported occupational exposures differed significantly between cases and controls ($p<0.001$). The mean number of years for exposure to dust and CGF was ~3–4 times higher among cases than controls (table 3). JEM cumulative exposure-years for biological dust exposure were significantly different between cases and controls, and marginally so for CGF exposure.

Table 2 Frequent job descriptions reported by cases and controls

Job description*	Jobs among cases n (%) (n=340)	Jobs among controls n (%) (n=221)
Administrative	41 (12)	47 (21)
Machinist (textile and shoe)	30 (9)	13 (6)
Builder	27 (8)	6 (3)
Driver	19 (6)	22 (10)
Fitter and turner	19 (6)	4 (2)
Operator	18 (5)	17 (8)
Painter	16 (5)	0 (0)
Supervisor	14 (4)	8 (4)
Welder	12 (3)	2 (1)
Maintenance	10 (3)	0 (0)
Manager	9 (3)	17 (8)
Mechanic	6 (2)	5 (2)
Quality control	1 (0.3)	12 (5)
Other	118 (35)	68 (31)

*Participants generally had multiple jobs, and would be included across several of the jobs in the table.

Table 3 Employment history and occupational exposures among cases and controls

	Cases (n=110)	Controls (n=102)	p Value
Currently employed (n (%))	13 (12)	12 (12)	0.97
Currently unemployed (n (%))	95 (86)	80 (78)	0.98
Currently unemployed due to ill-health (n (%))	59 (54)	18 (17)	<0.001
Self-reported exposure measures			
Dust exposure (n (%))	79 (72)	28 (28)	<0.001
CGF exposure (n (%))	82 (74)	26 (25)	<0.001
Either dust or CGF exposure (n (%))	84 (77)	24 (23)	<0.001
Dust and CGF (n (%))	61 (55)	18 (17)	<0.001
Total dust years (mean (SD))	15.7 (14.7)	4.7 (9.2)	<0.001
Total CGF years (mean (SD))	14.0 (14.1)	3.5 (8.9)	<0.001
JEM cumulative exposure years			
Biological dusts (mean (SD))	19.8 (29.2)	11.5 (20.0)	0.01
Mineral dusts (mean (SD))	22.4 (36.1)	16.1 (32.1)	0.14
CGF (mean (SD))	42.7 (44.9)	35.4 (44.9)	0.06

CGF, chemicals, gases or fumes; JEM, Job Exposure Matrix.

Logistic regression models, adjusting for smoking, TB, age and sex, strongly supported exposure-related association with COPD. The adjusted ORs all suggested an increased risk for COPD (OR >1). This was more evident and consistent with the self-reported exposure variables. For the JEM variables, this was statistically significant only for the biological dust high exposure category and CGF low exposure category. A trend in ORs was observed from low to high categories for the self-reported exposures and for the JEM biological dust exposures (table 4).

Smoking history showed a strong association with COPD. The adjusted ORs for ever smokers was 5.0 (95% CI 1.9 to 12.9), 5.5 (95% CI 2.1 to 14.1) and 5.3 (95% CI 2.1 to 13.8) from the models with biological dusts, mineral dusts and CGF variables, respectively (not shown in tables).

The strongest association with COPD as evident from our models was for TB. Depending on the model, ORs for TB ranged from 7.7 to 8.1 adjusted for age, gender, smoking status and exposure.

The PAR% for COPD was 25% for self-reported high exposure to dusts and CGF, but much lower (2.3–14.6%) when the JEM variables were used.

DISCUSSION

This case–control study is among the few reported hospital-based studies showing an association between occupational exposures and COPD. The findings in our study are particularly significant given the high prevalence of TB in the population from which our participants were drawn. The presence of the exposure–COPD relationship after adjusting for both smoking and TB confirms the association of COPD with dust exposure in this sample.

The almost twofold increased ORs for high cumulative exposure to biological dust, adjusted for smoking and past history of TB, is generally in keeping with the findings reported in other studies, particularly among North American and European populations.[22–24] The latter studies reported ORs from 1.3 to 3.1, compared with our study, ranging from 1.1 to 2.2 depending on the exposure type.

Table 4 Adjusted ORs for chronic obstructive pulmonary disease from logistic regression models*

	Cases (n (%))	Controls (n (%))	ORs (95% CI)	PAR%
Self-reported exposure				
Dusts				
Unexposed	49 (45)	76 (74)	1	
Low exposure-years	27 (25)	13 (13)	4.6 (1.9 to 10.8)	19.6
High exposure-years	34 (31)	14 (14)	5.9 (2.6 to 13.2)	25.7
Chemicals, gases and fumes				
Unexposed	41 (37)	72 (70)	1	
Low exposure-years	32 (29)	15 (15)	2.9 (1.3 to 6.3)	18.9
High exposure-years	37 (34)	16 (15)	3.6 (1.6 to 7.9)	25.6
Job exposure matrix exposure measures				
Biological dusts				
Unexposed	39 (35)	50 (49)	1	
Low cumulative exposure	27 (25)	25 (24)	1.3 (0.6 to 2.9)	5.5
High cumulative exposure	44 (40)	27 (26)	2.1 (1.1 to 4.2)	13.6
Mineral dusts				
Unexposed	46 (42)	51 (50)	1	
Low cumulative exposure	27 (25)	25 (24)	1.3 (0.6 to 2.7)	5.5
High cumulative exposure	37 (34)	26 (25)	1.1 (0.6 to 2.4)	2.3
Chemicals, gases and fumes				
Unexposed	21 (19)	36 (35)	1	
Low cumulative exposure	44 (40)	33 (32)	2.2 (1.1 to 4.7)	17.5
High cumulative exposure	45 (41)	34 (33)	1.8 (0.8 to 3.9)	14.6

*Models adjusted for age, sex, current smoker, ex-smoker, history of tuberculosis

There was limited evidence of correlation between the various exposure measures, but when regression models included multiple exposure variables, the effect estimates became smaller, and CIs widened.

Although the estimates reported in our study are generally in keeping with those reported from other international studies, our findings are particularly striking because of its control for TB—a disease of high prevalence within the population from which our sample was drawn. Studies have repeatedly reported the elevated risk for the development of COPD in those with a past history of TB.[13–15] A recent Chinese study of airflow obstruction and TB reported an increased age-, smoking- and occupational dust-adjusted risk for airflow obstruction among those with prior TB (OR 1.37; 95% CI 1.1 to 1.7). Occupational dust exposure in the longest job held did not change the risk for prior TB.[15] The rate of TB among South Africans is among the highest in the world, with an incident rate of 948/100 000 population.[25] Thus, smoking and TB are considered to be the leading causes of COPD in South Africa.[26] TB and non-specific occupational exposure have also been shown to be independent risk factors for chronic bronchitis[26] and chronic wheeze[27] in the South African population. Our study, in adjusting for these factors, provides additional evidence for the role of dusts, chemicals, gases, vapours and fumes in the development of COPD.

This study has a number of strengths that provide confidence in the findings. The case–control design, with cases being defined through a pulmonologist assessment, selected from specialist respiratory clinics, using clinical and lung function parameters according to the GOLD criteria, limits possible disease misclassification. The selection of non-respiratory specialist clinic-based controls, under the care of internal medicine specialists, who clinically excluded diagnoses of chronic respiratory disease, also limits disease misclassification Our ability to obtain detailed lifetime occupational histories permitted the determination of relatively precise exposure metrics, and together with the use of a COPD-validated JEM reduced possible bias in our exposure assessment. In recruiting COPD cases from specialist pulmonology clinics, this study probably has an advantage over population-based studies which are dependent on patient-based responses for the classification of outcome.[22 28]

There were several limitations to our study. Our decision to select patients presenting to specialist respiratory clinics in the public sector hospitals created a strong selection bias. First, because of the access to high standards of private medical care available for those with health insurance in South Africa, patients presenting to the public sector come from a narrow and low socio-economic band. The socio-economic variables collected during the study were employment status, home ownership and energy source, and these did not differ between cases and controls. We did not adjust for use of biomass fuels in this study, a known factor in the development of COPD in the developing world. Controls were selected from specific chronic diseases clinics, and therefore were not representative of the general population. Generally patients with moderate to severe disease (69% of cases were in GOLD III and IV stages), refractory to medical management from primary care medical practitioners, are referred to these specialist centres. Thus our findings are not generalisable to the broader population with COPD, but serve to affirm the association of occupational dust exposure with COPD. By definition, all potential controls with COPD and chronic bronchitis, asthma or emphysema were excluded, and this could have reduced the number of controls with TB inasmuch as TB is related to these chronic diseases. However, from all those eligible to become controls (ie, patients from non-respiratory chronic diseases clinics meeting the age and gender criteria) no more than 5% were screened out on the basis of having these diagnoses. Thus the under-representation of TB among the controls is not likely to have been substantial.

Additionally, our study may not be comparable with the broader blue collar working population in South Africa, because of the minimal mining exposure among our sample. The province, and particularly the cities, from which this sample was drawn are largely outside the key mining centres of South Africa. This lack of mining exposure is important because of our interest in TB. TB is on the causal pathway for COPD among those exposed to silica dust. While the absence of mining in our sample reduces this exposure, its presence in other industries such as sandblasting, welding and building could be a contributory factor. In our sample, <10% reported working in these industries, and no participant admitted to having had silica exposure.

Our small sample size, together with the small number of never-smokers particularly among the cases, is an important limitation. We were not able to investigate the risk by smoking status satisfactorily.

Another limitation was the lack of verification of the occupational history reported by the patients. Because most patients were recalling histories that dated back some 20–30 years ago, it is likely that this may have been reported erroneously. It is, however, documented that workers' recollection of dust exposure correlated well with actual dust sampling in the workplace.[29 30] A recall bias may have existed if such errors were more likely to have been present in the reporting by cases as compared with controls. It is very possible that those with COPD were more likely to recall and report working in environments with respiratory irritants. This is supported by effect estimates from models, with the self-reporting of exposure being much higher than estimates using JEM exposure measures. It is

likely that the use of this JEM, previously used in population-based COPD studies, adjusted for the recall bias that may have been present.[8 20]

There are likely to be disadvantages to the ALOHA JEM, but it is not likely to be substantially different from any other JEM, or developing one specific for this population.[31] Expert- and task-based information does not necessarily lead to better exposure asssessment.[32] Expert-based assessment depending on self-reports or self-reported exposure has, however, the additional problem of differential misclassification because of responder bias. A JEM is not likely to suffer from this.

In conclusion, our study not only lends support to the growing body of literature associating workplace exposures with COPD, but also suggests that among a population with a high prevalence of TB and cigarette smoking, occupational exposures remain an important factor. Controlling workplace exposures, together with antismoking and TB prevention programmes, is important if the increasing global prevalence of COPD is to be addressed.

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Competing interests None.

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