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## Research Article

# Chronic Obstructive Pulmonary Disease and Occupational Exposures: Epidemiological Evidence from R. Macedonia

### Abstract

**Introduction:** The research found consistent associations between workplace exposures across a wide range of sectors and the development of chronic obstructive pulmonary disease (COPD) independently of or in concert with cigarette smoking.

**Objective:** To present the epidemiological evidence for COPD among never-smoking workers from occupations associated with exposure to dusts, gases and/or fumes (dusty occupations) performed in R. Macedonia in the period 2011-2015.

**Methods:** Prevalence and characteristics of COPD were assessed in the groups of bricklayers, cotton workers, grain workers, dairy farmers, and welders. In addition, an equal group of administrative workers matched to dusty occupation workers by age and smoking status were studied as a control. Each study was performed by the same study protocol including questionnaire for respiratory symptoms in the last 12 months, baseline and post-bronchodilator spirometry and COPD diagnosis.

**Results:** The prevalence of overall and particular respiratory symptoms in the last 12 months was higher in the dusty occupation groups as compared to their prevalence in the groups of matched administrative workers. The mean values of all measured spirometric parameters, both baseline and post-bronchodilator, were lower in the dusty occupation groups than in the groups of matched administrative workers. The prevalence of COPD was significantly higher in the dusty occupation groups as compared to its prevalence in the groups of matched administrative workers, varying from 10.7% in dairy farmers, 10.8% in grain workers, 11.4% in cotton workers, 14.9% in bricklayers to 15.2% in welders. At the same time the COPD prevalence in the groups of matched administrative workers varied from 2.3% to 4.3%. COPD in all examined groups was close related to age over 45 years, as well as to duration of employment over 20 years in dusty occupation groups.

**Conclusion:** Findings from the presented studies indicated that certain occupational exposures may be associated with the development of COPD. Findings from the presented studies also indicated a need of implementation of adequate preventive measures in order to protect respiratory health of exposed workers.

## Introduction

Respiratory diseases rank as the third most prevalent work-related diseases (after ergonomic and stress-related diseases) according to a survey of occupational diseases in the European Union. Work-related asthma (WRA) is the most common work-related lung disease in the last decades, causing significant morbidity, disability and high costs [2]. In addition, the development of COPD as a consequence of workplace exposure is a matter of growing interest. Although the cigarette smoking is the major risk factor of COPD, there is consistent evidence that a substantial proportion of COPD cases cannot be explained by smoking. Other noxious particles and gases, such as workplace dusts, vapors, fumes or gases, indoor air pollution from burning biomass fuels from cooking and heating and urban outdoor air pollution are important risk factors of COPD. By systematic review of the articles in this domain, American Thoracic Society in 2003 has published the Statement for the occupational burden of airway disease (asthma, COPD, and organic dust-induced

asthma-like disorder) in which the prevalence of COPD attributable to workplace exposures was estimated as 15% from all COPD cases [3,4].

The research found consistent associations between workplace exposures and the development of COPD independently of or in concert with cigarette smoking, across a wide range of sectors, describing a nearly uniform pattern of exposure-response relationships. Based on the research, affected occupations include miners, construction workers, road workers, tunnel workers, welders, glass workers, metal workers, foundry workers, textile workers, farm laborers, wood workers, chemical workers, and rubber workers, i.e. a working population including millions and millions workers worldwide. In addition, existing evidence indicate that workplace exposure may influence the course of COPD as factors with important impact on the progression and severity of the disease. As in the case when the occupational agents are causative factors of COPD, the mechanisms underlying this effect still are not fully understood [5-7].

Up to date, several terms, such as occupational COPD, work-related COPD, occupationally-related COPD, industrial bronchitis, irritant-induced COPD, etc., were used to designate the role of the workplace exposure in the COPD development, but none of them is not widely appreciated. Namely, COPD does not have a clinical subcategory that is clearly identified as occupational, largely because the condition develops slowly and, given that the airflow limitation is persistent and progressive, does not reverse when exposure is discontinued. Thus, a clinical diagnosis of occupational COPD using methods similar to those employed for occupational asthma (OA) is not feasible. In addition, there are difficulties to differ the impact of cigarette smoking from that of workplace exposures in the COPD development. From these reasons the impact of workplace exposure on the development of the disease is based on the observed excess occurrence of COPD in certain occupations (epidemiological evidence), as well as on the findings of experimental studies (experimental evidence) [8,9].

## Methods

The present study is a report of the epidemiological evidence for COPD among never-smoking workers from occupations associated with exposure to dusts, gases and/or fumes (dusty occupations), i.e. bricklayers, cotton workers, grain workers, diary farmers, and welders. All workers from the certain occupation group worked in the same plant, i.e. cotton workers worked in one weaving plant, welders in one metallurgic plant, etc. The studies were performed in the period 2011-2015 at the Institute for Occupational Health of R. Macedonia, Skopje – World Health Organization Collaborating Center and GA2LEN Collaborating Center.

Each study was performed by the same study protocol including questionnaire for respiratory symptoms in the last 12 months, baseline and post-bronchodilator spirometry and COPD diagnosis.

The group of bricklayers included 47 male workers aged 34 to 57 years, employed in a big company for surface construction with duration of employment 12 to 28 years. Their working tasks included building of structures from individual units laid in and bound together by mortar. In addition, an equal group of never-smoking male office (administrative) workers matched to construction workers by age was studied as a control [10].

The group of cotton workers included 44 female workers (aged 36 to 56 years) employed in a manufacture producing cotton clothing with duration of employment 14 to 26 years. In addition, an equal group of never-smoking female administrative workers matched to the cotton spinners by age was studied as a control [11].

The group of grain workers consisted of 37 males aged 38 to 61 years with duration of employment 15 to 29 years. Their working tasks included cleaning, dressing and drying grain (wheat, rye, oats and corn), as well as transferring grain in or out of grain stores. In addition, an equal group of male office workers matched to the grain workers by age and smoking status was studied as a control [12].

The group of diary farmers consisted of 52 males aged 26 to 59 years with duration of employment 5 to 40 years. Their working tasks included preparation of fodder feeding and animal meals, milking,

staying in the barn, cattle rising, preparation of straw, and taking care for milk hygiene and animals health. In addition, an equal group of male administrative workers matched to the diary farmers by age and duration of employment were studied as a control [13].

The group of welders included 46 males aged 37 to 59 years employed as stainless steel welding workers with duration of exposure 14 to 27 years. In addition, an equal group of male administrative workers matched to the welders by age and smoking status was studied as a control [14].

All examined workers were never smokers, i.e. non-smokers who have never smoked at all, or have never been daily smokers and have smoked less than 100 cigarettes in their lifetime [15,16].

Respiratory symptoms in the last 12 months were assessed using the European Community for Coal and Steel questionnaire (ECCS-87), and the European Community Respiratory Health Survey (ECRHS) questionnaire [17,18]. The work-relatedness of the respiratory symptoms was defined as more than usual cough, phlegm, dyspnea, wheezing, and chest tightness during daily work [19].

The baseline spirometry, including measures of forced vital capacity (FVC), FEV1 (forced expiratory volume in 1 second), FEV1/FVC ratio, and maximal expiratory flow at 50%, 25%, and 25-75% of FVC (MEF50, MEF25, and MEF25-75, respectively), was performed and interpreted according to the actual recommendations of European Respiratory Society (ERS) and American Thoracic Society (ATS) [20,21].

Bronchial reversibility testing was performed according to the actual Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) spirometry guide (4X). The degree of FEV1 reversibility was expressed as % FEV1 reversibility ( $[\text{post-bronchodilator FEV1} - \text{pre-bronchodilator FEV1}] / \text{pre-bronchodilator FEV1} \times 100$ ). Significant FEV1 improvement (a change more than 12% and more than 200 mL) in the presence of fixed airflow limitation did not negate a diagnosis of COPD.

The diagnosis of COPD was established according to the recent GOLD recommendations, i.e., COPD was considered by the presence of a post-bronchodilator FEV1/FVC less than 0.70 (its value indicating persistent airflow limitation) in the subjects who had dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease (tobacco smoke, smoke from home cooking and heating fuels, and/or occupational dusts and chemicals) [22].

## Results

The prevalence of overall respiratory symptoms in the last 12 months in dusty occupation workers was similar varying from 36.5% in diary farmers to 44.7% in bricklayers (Figure 1). At the same time, the prevalence of overall respiratory symptoms in the last 12 months in the groups of administrative workers (i.e. matched controls) varied from 23.1% to 26.1%.

The highest prevalence of particular respiratory symptoms in the last 12 months in all dusty occupation groups was registered for cough (varying from 26.1% in welders to 35.1% in grain workers), phlegm

(varying from 13.5% in grain workers to 19.2% in dairy farmers) and dyspnea (varying from 13.0% in welders to 18.2% in cotton workers). The highest prevalence of particular respiratory symptoms in the last 12 months in the different groups of administrative workers was registered for cough (varying from 8.7% to 22.5%) and chest tightness (varying from 5.8% to 12.8%).

The mean values of all measured spirometric parameters, both baseline and post-bronchodilator, were lower in dusty occupation groups as compared to their values in the groups of matched administrative workers. In addition, mean post-bronchodilator values of all measured spirometric parameters were higher in all examined groups but significant difference was not registered in none of them. **Figure 2** is shown mean baseline and post-bronchodilator values of FEV<sub>1</sub> in dusty occupation groups.

The prevalence of COPD in dusty occupation groups varied from 10.7% in dairy farmers to 15.2% in welders (**Figure 3**). At the same time, the COPD prevalence in the groups of matched administrative workers varied from 2.3% to 4.3%. The difference in the COPD prevalence registered for each dusty occupation group was significantly higher as compared to its prevalence in the each group of matched administrative workers.

The prevalence of COPD in all examined groups (i.e. all dusty occupation groups, as well as all groups of matched administrative workers) was significantly higher in the workers aged more than 40 years than in the workers aged less than 45 years. In addition, the prevalence of COPD in all dusty occupation groups was significantly higher in the workers with duration of employment more than 20 years as compared to its prevalence in workers employed less than 20 years.

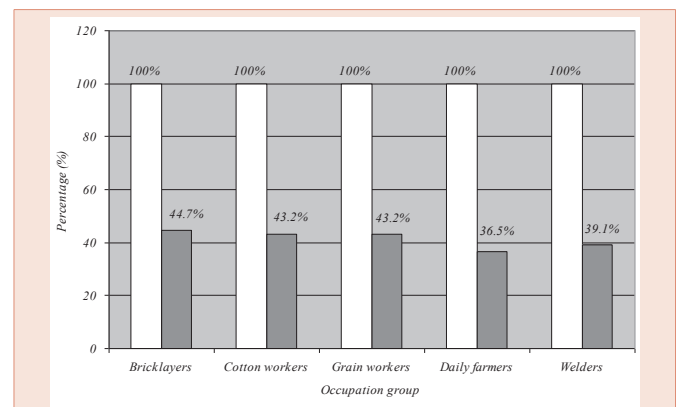
## Discussion

Chronic obstructive pulmonary disease (COPD) represents one of the principal demands of the public health at global level due to high morbidity, early mortality, high date rates and significant costs to health systems. The projection of the Global Burden of Disease Study indicates that COPD in 2020 will be the third leading cause of death worldwide (from sixth in 1990) and fifth leading cause of years lost (disability-adjusted life years - DALYs) through early mortality or handicap (12th in 1990) [23].

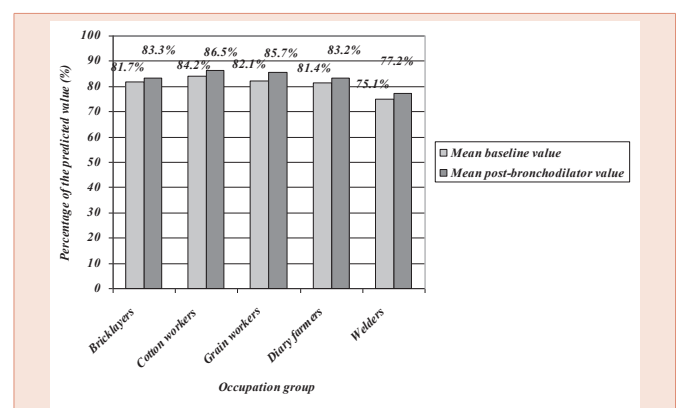
Cigarette smoking is the major risk factor for COPD. However, smoking explains no more than two-thirds of the variation in COPD prevalence in epidemiological studies, and often less. The non-smokers are also at risk for developing COPD. Workplace exposures to dusts, vapors, fumes and gases are established as risk factors by studies of many worker groups. As it is mentioned above, according to the ATS Statement for the occupational burden of airway disease, workplace exposures are responsible for around 15% of COPD overall but their influence is likely to vary depending on their nature and extent and may be much higher in some areas. The existing evidence suggests that workplace exposures contribute substantially to the COPD development and might continue to do so unless carefully controlled and regulated [24,25].

The evidence that workplace exposures may be causally related to COPD comes from epidemiological studies being based on the

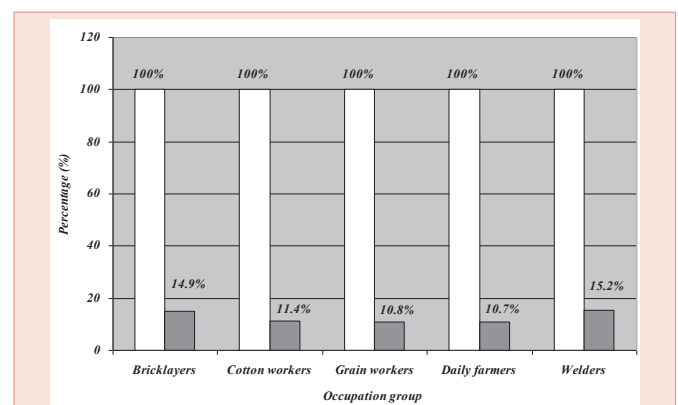
observed excess occurrence of COPD in certain occupations. Further evidence that occupational agents are capable to induce COPD comes from experimental studies, particularly in animal model. The epidemiological studies are divisible into population-based studies (community-based studies) with population with diverse occupations



**Figure 1:** The prevalence of overall respiratory symptoms in the last 12 months in the dusty occupation groups.



**Figure 2:** Mean baseline and post-bronchodilator values of FEV<sub>1</sub> in dusty occupation groups.



**Figure 3:** The prevalence of COPD in dusty occupation groups.

and hence exposures, and studies that examine particular workplaces and industries, with relatively homogenous exposures (workplace-based studies). The majority of epidemiological are cross-sectional in design and so open to concerns over cause and effect arising, e.g. from healthy workers effect (HWE).

The present study is a review of the results of the cross-sectional analysis from five workplace-based studies regarding the prevalence and characteristics of COPD among non-smoking workers in certain occupations in R. Macedonia. Each study included a group of workers from dusty occupation (bricklayers, cotton workers, grain workers, diary farmers, and welders) and a group of matched administrative workers. As the authors of these studies aimed at excluding the effect of smoking on the COPD development, they examined only never-smoking workers (besides option to include smoking workers and to use regression analyses), so the examined groups included relatively small number of study subjects.

An excess occurrence of respiratory symptoms in each dusty occupational group as compared to their occurrence in the group of matched administrative workers was registered. Similar findings, i.e. an excess of acute and chronic respiratory symptoms in workers with similar occupational exposures are reported in a number of studies performed in Europe and North America including similar occupational exposures (i.e. concrete dust, textile dust, grain dust, etc.) [26-30]. Despite the presence of chronic respiratory symptoms did not always match the level of lung function impairment, the mean values of all measured spirometric parameters, both baseline and post-bronchodilator, in dusty occupation groups were lower than their mean values in the groups of dusty occupation workers. These findings confirmed the findings from several studies performed in the last decades, that occupational exposure to inorganic or organic dust is associated with chronic airflow obstruction independent of cigarette smoking and separate from other effects of exposure such as pneumoconiosis, asthma or hypersensitivity pneumonitis [31-34].

The prevalence of COPD registered in the dusty occupation groups was between three- and five-fold higher than its prevalence registered in the groups of matched administrative workers, varying from 10.7% in diary farmers to 15.2% in welders. In addition, the prevalence of COPD in the groups of administrative workers varied from 2.3% to 4.3%. The prevalence of COPD in all examined groups was close related to age over 45 years. At the same time, the prevalence of COPD in all dusty occupation groups was close related to duration of employment over 20 years suggesting dose-response relationship. Findings from several studies indicated dose-response relationship between lung function impairment and occupational exposure to inorganic dust COPD [35,36]. Furthermore, significantly higher COPD prevalence in dusty occupation workers than in administrative workers registered in the reviewed studies confirm the association between occupational exposures to dusts, gases and/or fumes and COPD development, i.e. these findings support the observations that cigarette smoke and some forms of inorganic and organic dust contain the same pro-inflammatory agents and trigger the same effector molecule in the airways. In the case-control study aimed to ascertain the risk of COPD in male workers in different occupation groups with respect to administrative workers as a reference group,

Mastrangelo et al. [37], found that age, smoking (both current and former habit), the average cigarettes number, as well as occupational factors were strong risk factors for COPD. The reported age-smoking adjusted odds ratios (ORs) for COPD ranged from 15.1 in farmers, 12.1 in foundry workers, 7.2 in cotton workers, 6.4 in welders, 6.5 in refractory brick workers, 4.7 in painters to 3.1 in construction workers.

The findings of the reviewed studies are subjects to several limitations. First, relatively small number of the subjects in the study groups could have certain implications on the data obtained and its interpretation. Second, environmental measurements were not performed, so the effects of the nature and the extent of occupational exposure on COPD in any of the analyzed studies could not be documented. The third limitation is the gender differences in the examined groups, i.e. four dusty occupation groups and their matched controls included only males and one group (cotton workers) and its matched controls included only females. As some studies suggested that women are more susceptible to the effects of tobacco smoke and other noxious particles and gases than men, the results from the study with cotton workers may be not comparable to results of the studies with other dusty occupation groups [38].

Last but not least limitation of the studies is their cross-sectional design which enables identifying associations rather than cause-and-effect relationships. In addition, as in the case of any cross-sectional study, the impact of the HWE on the data obtained could not be excluded, as it is mentioned above. On the other side, most of the evidence of an association between occupational exposures and COPD is available in cross-sectional studies on groups of workers with specific jobs and/or exposures. The strength of the analyzed studies is the extensive investigation of respiratory effects of occupational exposure on never-smoking workers performing specific activity within the different occupations.

## Conclusion

In conclusion, results of the analyzed studies indicated three- to five-fold higher prevalence of COPD in dusty occupation groups as compared to its prevalence in matched administrative workers. COPD in all examined groups was close related to age over 45 years, as well as to duration of employment over 20 years in dusty occupation groups. These findings confirmed that certain occupational exposures may be associated with the development of COPD independently of cigarette smoking. These findings also indicated the need of implementation of adequate preventive measures in order to protect respiratory health of exposed workers.

## Authors Participations

JM participated in the study design, writing the protocol, data collection, managing the analyses of the study, and writing all versions of the manuscript. JKB participated in the study design, writing the protocol, managing the analyses of the study, as well as writing all versions of the manuscript. KV participated in the managing of the analyses of the study. SS and DM participated in the data collection and in the managing of the analyses of the study. All authors read and approved the final manuscript.

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