The Turkish Journal of Occupational / Environmental Medicine and Safety
Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

Chronic obstructive pulmonary disease in never-smoking male workers exposed to grain dust

Jordan Minov[1], Jovanka Karadzinska-Bislimovska[1], Engin Tutkun[2], Kristin Vasilevska[3], Saso Stoleski[1], D. Mijakoski[1]
[1] Institute for Occupational Health of R. Macedonia, R. Macedonia
[2] Ankara Occupational Diseases Hospital, Ankara, Turkey
[3] Institute for Epidemiology and Biostatistics, Skopje, R. Macedonia

Jordan B. Minov, MD PhD
Department of Cardiorespiratory Functional Diagnostics
Institute for Occupational Health of R. Macedonia – WHO Collaborating Center and GA²LEN Collaborating Center
II Makedonska Brigada 43
1000 Skopje, R. Macedonia
Tel: + 389 2 2639 637
Fax: + 389 2 2621 428
e-mail: minovj@hotmail.com

Abstract

Introduction. Existing literature indicates that workplace exposure to grain dust is associated with adverse respiratory effects in exposed workers. **Aim of the study**. To assess prevalence and characteristics of chronic obstructive pulmonary disease (COPD) in workers exposed to grain dust. **Material and methods.** We performed a cross-sectional study including 37 never-smoking male grain workers and an equal number of male office workers matched to grain workers by age and smoking status studied as a control. Evaluation of examined subjects consisted of completion of a questionnaire, baseline spirometry, and bronchodilator reversibility testing. **Results.** We found higher prevalence of respiratory symptoms in grain workers with significant difference for cough and phlegm. Majority of respiratory symptoms in grain workers were work-related. The mean values of all measured spirometric parameters were significantly lower in grain workers. The prevalence of COPD, diagnosed by spirometric confirming of persistent airflow limitation, was significantly higher in grain workers as compared to office workers (10.8% *vs.* 2.7%, *P* = 0,021).COPD in grain workers was close related to age over 45 years and duration of employment at the actual workplace over 20 years. **Conclusions.** Our findings suggest relationship between workplace exposure to grain dust and persistent airflow limitation in exposed workers.

Key words: airflow limitation, baseline spiroemtry, bronchodilator reversibility testing, grain workers, office workers, questionnaire, workplace exposure.

As the frequency of the mineral dust-induced pnumoconioses decreased primarily due to the control of exposure, the obstructive airway diseases, i.e. asthma and chronic obstructive pulmonary disease (COPD), became the most prevalent work-related lung diseases.

Although cigarette smoking is considered as a major factor for the COPD development and progression, minority of smokers (around 15%) develop clinically significant COPD, suggesting that genetic predisposition and other exogenous factors are required for the development of lung injury (1). According to the American Thoracic Society (ATS) Statement for the occupational burden of airway disease (asthma, COPD, and organic dust-induced asthma-like disorder), the prevalence of COPD attributable to workplace exposures is around 15% from all COPD cases (2). In addition, the population attributable fraction (PAR) for COPD attributable to work is estimated at 19% overall and 31% among never-smokers (3). There is no doubt that certain workplace exposures enhance the risk of COPD and may do so independently of or in concert with cigarette smoking. The evidence is most coherent for work that entails exposure to coal, silica, welding fume, cadmium fume, cotton dust, farming dusts, grain dust or wood dust (4).

Grain dust is the dust produced from the harvesting, drying, handling, storage or processing of barley, wheat, oats, maize or rye and includes any contaminants or additives within the dust (e.g. bacteria, endotoxins, fungal spores, insects and insect debris, pesticide residues, silica from the soil, etc.). Processes that create grain dust include: harvesting grain and transferring grain from combines into trailers; cleaning, dressing and drying grain; moving grain about in a grain store; transferring grain in or out of grain stores or terminals; milling and mixing dry grain; feeding dry milled grain; maintenance of plant and equipment; cleaning of buildings, vehicles, plant and equipment using compressed air or by manual/mechanical sweeping; and silo cleaning. Workplace exposure to grain dust is associated with adverse health effects, such as eye and skin irritation (i.e. conjunctivitis and skin rashes), as well as respiratory effects (rhinitis, asthma, chronic bronchitis, COPD, extrinsic allergic alveolitis, and organic dust toxic syndrome) (5).

Experimental evidence demonstrates in an animal model that exposures to organic dusts (e.g. cotton dust or corn dust) containing endotoxin or lipopolysaccharide (LPS), i.e. a heat-stable toxin associated with the outer membranes of certain Gram-negative bacteria ubiquitous in the environment, over time may share some common mechanisms of COPD. In addition, findings from experimental studies also show that chronic treatment of rabbits and hamsters with intratracheal LSP instillation causes parenchymal architectural changes in the lung that are consistent with emphysema (6, 7).

In the present study we aimed at assessment of prevalence and characterstics of COPD in never-smoking male workers exposed to grain dust.

The Turkish Journal of Occupational / Environmental Medicine and Safety

Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

Materials and Methods

Study design and setting

A cross-sectional study was carried out at the Institute for Occupational Health of R. Macedonia, Skopje - WHO Collaborating Center for Occupational Health and GA^{2}LEN Collaborating Center in the period November 2014 - May 2015. Prevalence of chronic respiratory symptoms, mean values of spirometric parameters, and prevalence of COPD was compared between a group of never-smoking male grain workers and a group of never-smoking male office workers.

Subjects

We examined 37 male grain workers aged 38 to 61 years with duration of employment 15 to 29 years. They worked in two work shifts lasting 8 hours and 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. The process control provided keeping of the exposures at the permissible levels. The protective equipment during the working included protective clothing, gloves, glasses, and masks. All examined grain 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 (8, 9).

In addition, an equal group of male office workers matched to the grain workers by age and smoking status was studied as a control.

In either group there were no subjects with chronic respiratory disease diagnosed by physician (i.e. asthma, COPD, bronchiectasis, etc.), neither subject treated with bronchodilators and/or corticosteroids. In either group also there were no subjects in whom spirometry or bronchodilator reversibility testing was contraindicated (10, 11).

Questionnaire

An interviewer-led questionnaire was completed by all study subjects. The questionnaire included questions on work history (e.g., chronological list of jobs; description of job activities at the actual workplace; type, extent and duration of exposure; and use of protective equipment), respiratory symptoms in the last 12 months and their relatedness to the workplace, family history of COPD and CB (taking into account the first-degree relatives), environmental exposure to tobacco smoke (ETS), accompanying disease, and medication use.

Respiratory symptoms in the last 12 months (cough, phlegm, dyspnea, wheezing, and chest tightness) were documented using the European Community for Coal and Steel questionnaire (ECCS-87), and the European Community Respiratory Health Survey (ECRHS) questionnaire (12, 13). The work-relatedness of the respiratory symptoms was defined as more than usual cough, phlegm, dyspnea, wheezing, and chest tightness during daily work (14).

ETS or passive smoking was defined as an exposure to tobacco combustion products from smoking by others (at home, workplace, etc.), i.e. as a presence of at least one smoker in the household and/or in the workplace (15, 16).

The Turkish Journal of Occupational / Environmental Medicine and Safety
Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

Baseline spirometry

The baseline spirometry, including measures of forced vital capacity (FVC), FEV_1, FEV_1/FVC, and maximal expiratory flow at 75%, 50%, 25%, and 25-75% of FVC (MEF_{75}, MEF_{50}, MEF_{25}, and MEF_{25-75}, respectively), was performed in all subjects using spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany) with recording the best result from three measurements the values of FEV_1 of which were within 5% of each other. The results of spirometry were expressed as percentages of the predicted values according to the actual recommendations of European Repsiratory Society (ERS) and ATS (10, 11).

Bronchodilator reversibility testing

Bronchial reversibility testing was performed according to the actual Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometry guide (10). Spirometric measurements were performed before and 20 minutes after administration of 400 μg salbutamol by metered dose inhaler through spacer. Fixed airflow narrowing characteristic for COPD was considered if post-bronchodilator FEV_1/FVC remained less than 0.70. The degree of FEV_1 reversibility was expressed as % FEV_1 reversibility ([post-bronchodilator FEV_1 – pre-bronchodilator FEV_1] / pre-bronchodilator FEV_1 x 100). Significant FEV_1 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.

COPD diagnosis

The diagnosis of COPD was established according to the actual GOLD recommendations (17), i.e., COPD was considered by the presence of a post-bronchodilator FEV_1/FVC less than 0.70 suggesting persistent airflow limitation in the subjects who had dyspnea, chronic cough or sputum production, and a history of exposure to risk factors for the disease (noxious particles and gases, i.e. tobacco smoke, smoke from home cooking and heating fuels, and/or occupational dusts and chemicals).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows. Continuous variables were expressed as mean values with standard deviation (SD), and the nominal variables as numbers and percentages. Analyses of the data included testing the differences in prevalence, comparison of the means, and testing the association between COPD and studied variables. Chi-square test (or Fisher's exact test where appropriate) was used for testing difference in the prevalence. Comparison of spirometric measurements was performed by independent-samples *T*-test. Chi-square test was used for testing association between COPD and studied variables. A *P*-value less than 0.05 was considered as statistically significant.

The Turkish Journal of Occupational / Environmental Medicine and Safety
Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

Results

Demographic characteristics of the study subjects were similar in both examined groups (Table 1).

Table 1. Demographics of the study subjects

Variable	Grain workers (n = 37)	Office workers (n = 37)
Age (years)	46.1 ± 5.4	45.4 ± 4.9
Less than 45 years	17 (45.9%)	18 (48.6%)
More than 45 years	20 (54.1%)	19 (52.4%)
BMI (kg/m^2)	25.3 ± 1.8	26.1 ± 2.1
BMI less than 25	18 (48.6%)	17 (45.9%)
BMI more than 25	19 (52.4%)	26 (54.1%)
Duration of employment at the actual workplace (years)	19.2 ± 3.8	20.5 ± 3.4
Duration of employment less than 20 years	16 (43.2%)	19 (52.4%)
Duration of employment more than 20 years	21 (56.8%)	18 (48.6%)
Family history of COPD or CB	5 (13.5%)	4 (10.8%)
Exposure to ETS	14 (37.8%)	12 (32.4%)
Accompanying diseases		
Arterial hypertension	5 (13.5%)	7 (18.9%)
Diabetes mellitus type 2	2 (5.4%)	3 (8.1%)
Peptic ulcer	3 (8.1%)	3 (8.1%)

Numerical data are expressed as mean value with standard deviation; frequencies as number and percentage of study subjects with certain variable.
BMI: body mass index; kg: kilogram; m: meter; COPD: chronic obstructive pulmonary disease; CB: chronic bronchitis; ETS: enirinmental tobacco smoke.

Prevalence of overall respiratory symptoms in the last 12 months was higher in grain workers but statistical significance was not reached. In regard to the particular chronic respiratory symptoms, we registered significantly higher prevalence of cough and phlegm in grain workers (Table 2).

Table 2. Prevalence of respiratory symptoms in the last 12 months in the study subjects

Respiratory symptoms in the last 12 months	Grain workers (n = 37)	Office workers (n = 37)	*P*-value*
Overall respiratory symptoms in the last 12 months	16 (43.2%)	9 (24.3%)	0.122
Cough	13 (35.1%)	5 (13.5%)	0.042
Phlegm	5 (13.5%)	1 (2.7%)	0.014
Dyspnea	5 (13.5%)	3 (8.1%)	0.137
Wheezing	6 (16.2%)	4 (10.8%)	0.212
Chest tightness	5 (13.5%)	4 (10.8%)	0.254

Data are expressed as number and percentage of study subjects with certain variable.
*Tested by Chi-square test (or Fisher's exact test where appropriate).

The majority of respiratory symptoms in the last 12 months in the grain workers were related to their work (81.3%). The highest relatedness with workplace was reported for cough (76.9%) and phlegm (80.0%). Work relatedness of the symptoms was reported by 22.2% of the office workers with respiratory symptoms, i.e. by two office workers with cough.

The mean baseline values of all spirometric parameters were significantly lower in grain workers (Table 3).

Table 3. Mean baseline values of spirometric parameters in the study subjects

Spirometric parameter	Grain workers (n = 37)	Office workers (n = 37)	*P*-value*
FVC (%pred)	95.1 ± 9.1	97.3 ± 8.3	0.034
FEV_1 (%pred)	82.1 ± 8.2	85.2 ± 10.1	0.020
FEV_1/FVC	0.78 ± 0.04	0.82 ± 0.05	0.019
MEF_{75} (%pred)	68.6 ± 9.4	74.3 ± 11.2	0.008
MEF_{50} (%pred)	63.1 ± 10.9	69.4 ± 11.9	0.003
MEF_{25} (%pred)	54.4 ± 13.2	65.7 ± 12.8	0.000
MEF_{25-75} (%pred)	62.1 ± 14.3	73.4 ± 15.8	0.000

Data are expressed as mean value with standard deviation.
FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; MEF_{75}, MEF_{50}, MEF_{25}, MEF_{25-75}: maximal expiratory flow at 75%, 50%, 25% and 25-75% of FVC, respectively; % pred: % of predicted value.
*Compared by Independent-samples *T*-test.

The mean post-bronchodilator values of all spirometric parameters were also significantly lower in grain workers (Table 4). In addition, the mean FEV_1 reversibility (%FEV_1 reversibility) was significantly higher in grain workers (9.4% *vs.* 4.3%, P = 0.011; Independent-samples *T*-test).

Table 4. Mean post-bronchodilator values of spirometric parameters in the study subjects

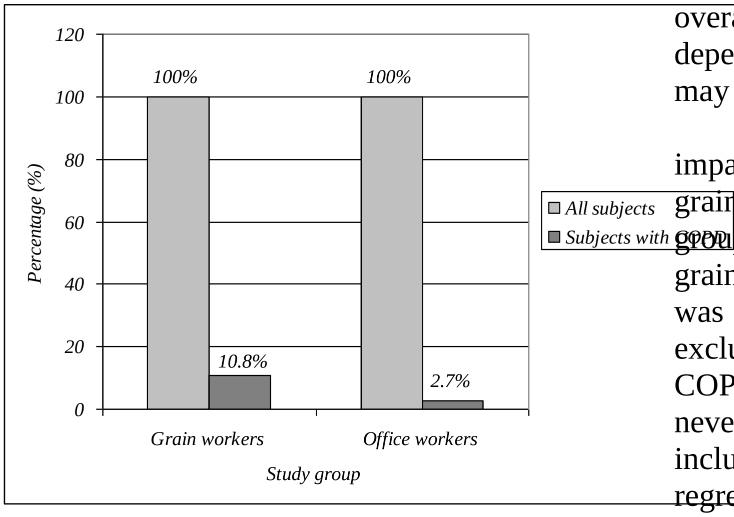
Spirometric parameter	Grain workers (n = 37)	Office workers (n = 37)	*P*-value*
FVC (%pred)	95.9 ± 10.7	98.1 ± 12.4	0.038
FEV_1 (%pred)	85.7 ± 11.8	88.9 ± 12.9	0.015
FEV_1/FVC	0.79 ± 0.06	0.83 ± 0.09	0.011
MEF_{75} (%pred)	70.6 ± 11.7	76.8 ± 8.9	0.000
MEF_{50} (%pred)	65.1 ± 12.9	72.8 ± 9.4	0.000
MEF_{25} (%pred)	57.1 ± 14.9	69.3 ± 10.8	0.000
MEF_{25-75} (%pred)	67.2 ± 13.8	75.8 ± 11.3	0.000

Data are expressed as mean value with standard deviation.
FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; MEF_{75}, MEF_{50}, MEF_{25}, MEF_{25-75}: maximal expiratory flow at 75%, 50%, 25% and 25-75% of FVC, respectively; % pred.: % of predicted value.
*Compared by Independent-samples *T*-test.

Four subjects among grain workers and one subject among office workers met criteria for diagnosis of COPD (10.8% *vs.* 2.7%, P = 0,021; Fisher's exact test) (Figure 1). All grain workers with COPD reported work-relatedness of their symptoms. According to the GOLD 2010 classification of COPD severity (18), all subjects with COPD can be categorized as a mild COPD (FEV_1/FVC < 0.70; $FEV_1 \geq$ 80% predicted).

Figure 1. Prevalence of COPD in the study subjects

The Turkish Journal of Occupational / Environmental Medicine and Safety
Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711



All COPD cases in both examined groups were aged more than 45 years and were employed at the actual workplace more than 20 years. Associations between COPD and other variables (e.g., BMI, family history of COPD or CB, and environmental ETS) were statistically non-significant in both grain workers and office workers.

Discussion

COPD remains frequent and costly disease currently representing one of the principal demands of the public health worldwide. 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) (19). As it is mentioned earlier, 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.

In the present study we assessed the impact of specific occupational exposure in grain workers on developing of COPD. A group of male office workers matched to grain workers by age and smoking status was studied as a control. As we aimed at excluding the effect of smoking on the COPD development, we 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. The examined groups included subjects with similar demographic characteristics. In either group there was a large proportion of passive smokers (over 30%) that is similar to its prevalence among workers in R. Macedonia documented in our previous studies (20, 21) indicating insufficient nationwide smoking cessation activities.

As it is mentioned earlier, the dust to which grain workers are exposed is complex, whether it is wheat, barley, oats, corn or rye. It consists of the grain, hairs from the epicarp and the germ. Plant contaminants include weeds and pollens. Fungi grow in grain depending on its freshness. Rodents often infest it, leaving their spoor. In addition, chemicals are usually added to control fungi, insects and rodents. Free silica from the soil may be present or incorporated into the plant as phytoliths. Finally, grain workers often handle oil seeds such as sunflower, flax and mustard (22).

We found higher prevalence of respiratory symptoms in the last 12 months in grain workers than in office workers with

The Turkish Journal of Occupational / Environmental Medicine and Safety
Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

significantly higher prevalence of cough and phlegm. The majority of respiratory symptoms in grain workers were work-related, reaching around 80% for cough and phlegm. An excess of respiratory symptoms (either acute or chronic) were documented in several studies in grain workers, e.g. in a series of studies conducted in Canadian grain workers in the last four decades (23-27).

The mean values of all measured spirometric parameters in the present study (FVC, FEV_1, FEV_1/FVC, MEF_{75}, MEF_{50}, MEF_{25}, and MEF_{25-75}) were significantly lower in grain workers as compared to their mean values in office workers. Similar findings were reported in several cross-sectional and longitudinal studies on respiratory effects of workplace exposure to grain dust, e.g. in the studies conducted in Canadian grain workers mentioned earlier. Furthermore, in a Dutch longitudinal study with five year follow-up including around 2,000 workers in the grain processing and animal feed production, Post et al. found a significant decline in FEV_1 in the highest exposed workers compared with no and lowest exposed (28). In a study aimed at improvement of the dust control measures in the grain industry in Egypt including 200 flour mill workers, Mohammadien et al. found significantly lower mean values of FVC, FEV_1, FEV_1/FVC, MEF_{75}, MEF_{50}, and MEF_{25} in flour mill workers than in unexposed controls with clear dose-response relationship (29).

We performed bronchodilator reversibility testing in order to detect subjects with the presence of a post-bronchodilator FEV_1/FVC less than 0.70, i.e., to confirm the diagnosis of COPD. According to the actual GOLD recommendations, the post-bronchodilator spirometry is required for diagnosis and assessment of severity of COPD, but the degree of reversibility of airflow limitation (e.g., FEV_1 measurements before and after administration of bronchodilator) is no longer recommended. The degree of reversibility has not be shown to add to the diagnosis, differential diagnosis with asthma, or to prediction of the response to long-term treatment with bronchodilators or corticosteroids (17). We found significantly higher prevalence of COPD among grain workers than in office workers, i.e. the COPD prevalence in grain workers was fourfold higher than its prevalence in office workers. COPD in grain workers was close related to age over 45 years and duration of employment at the actual workplace over 20 years probably reflecting the sum of cumulative exposures throughout the life in susceptible subjects. Similarly, in a South African longitudinal study with a six year follow-up including 159 milling workers, Bachmann & Myers found three-fold higher prevalence of airflow limitation (defined as $FEV_1/FVC < 0.7$) among the highest exposed workers compared with the lowest exposed workers (30). In addition, these findings correspond with findings from our former studies on COPD prevalence in never-smoking workers exposed to silica dust and cotton dust indicating the role of the workplace exposures to mineral and organic dust as a risk factor for COPD (31, 32).

The present study had some limitations. First, relatively small number of the subjects in the study groups could have certain implications on the data obtained and

The Turkish Journal of Occupational / Environmental Medicine and Safety
Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

its interpretation. Second, as in the case of any cross-sectional study, the impact of healthy workers' effect on the data obtained could not be excluded. The healthy-workers' effect (HWE) is the most common selection bias in occupational studies occurring because relatively healthy individuals are likely to gain employment and to remain employed and it may partially or completely mask excess mortality and morbidity caused by harmful exposure. Third, environmental measurements were not performed, so we could not document the effect of the type and the level of exposure on COPD. The strength of the study is the investigation of respiratory effects of the workplace exposure on never-smoking workers employed at the specific workplace within the grain industry.

Conclusions

In conclusion, in a cross-sectional study including never-smoking grain workers we found a higher prevalence of respiratory symptoms in the last 12 months, significantly highly mean values of spirometric parameters, and significantly higher prevalence of COPD than in matched office workers. COPD in grain workers was close related to age and duration of employment at the actual workplace. Our findings also indicated a need of improvement of preventive measures, i.e. proper engineering controls, respiratory protective equipment if engineering controls are not feasible and regular periodical medical examinations, in order to protect the health of exposed workers.

Competing Interests
All authors hereby have declared that no competing interests exist.

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. ET participated in the managing the analyses of the study and in the writing all versions of the manuscript. KV performed the statistical analysis and 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.

References:

1. Sezer H, Akkurt I, Guler N, et al. A case-control study on the effect of exposure to different substances on the development of COPD. Ann Epidemiol 2006; 16: 59-62.
2. Balmes J, Becklake M, Blanc P, et al. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med 2003; 167: 787-797.
3. Hnizdo E, Sullivan PA, Bang KM, Wagber G. Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study of data from the Third National Health and Nutrution Examination Survey. Am J Epidemiol 2002; 156: 738-746.
4. Cullinan P. Occupation and chronic obstructive pulmonary disease (COPD). British Medical Bulletin 2012; 104: 143-161.
5. American Conference of Governmental Industrial Hygienists. Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinati (OH): ACGIH, 2009.
6. Brass DM, Savov JD, Whitehead GS, et al. LPS binding protein is important in the airway response to inhaled endotoxin. J Allergy Clin Immunol 2004; 114: 586-592.
7. Savov JD, Gavett SH, Brass DM , et al. Neutrophils play a critical role in LSP-induced airway disease. Am J Physiol Lung Cell Mol Physiol 2002; 283: L952-L962.
8. World Health Organization. Guidelines for controlling and monitoring the tobbaco epidemic. Geneva, WHO, 1998.
9. Leffondre K, Abrahamowicz M, Siemiatycki J, Rachet B. Modelling smoking history: A comparison of different approaches. Am J Epidemiol 2002; 156: 813-823.
10. Spirometry Guide: 2010 Update. *http://www.goldcopd.org/uploads/users/files/GOLD_Spirometry_2010.pdf*. Accessed 09.07.2015.
11. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. Eur Respir J 2005; 26: 319-338.
12. Minette A. Questionnaire of the European Community for Coal and Steel (ECSC) on respiratory symptoms. 1987 - updating of the 1962 and 1967 questionnaires for studying chronic bronchitis and emphysema. Eur Respir J 1989; 2:165-177.
13. European Community Respiratory Health Survey. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Respiratory Health Survey (ECRHS). Eur Respir J 1996; 9: 687-695.
14. Meijer E, Grobbe DE, Heederik DJJ. Health surveillance for occupational chronic obstructive disease. J Occup Environ Med 2001; 43: 444-450.
15. U.S. Department of Health and Human Services. The health consequences of smoking: chronic obstructive pulmonary disease. A report of the Surgeon General. US Department of Health and Human Services, Public Health Service, Office of the Assistant for Health, Office of Smoking and Health. DHHS Publication No. 84-50 205, 1984.

16. Janson C, Chinn S, Jarvis D, Zock JP, Toren K, Burney P, for the European Community Respiratory Health Survey. Effects of passive smoking on respiratory symptoms, bronchial responsiveness, lung function, and total serum IgE in the European Community Respiratory Health Survey: a cross-sectional study. Lancet 2001; 358: 2103-2109.
17. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: Updated 2015. Available at: *http://www.goldcopd.org/uploads/users/files/GOLD_Report_2015_Feb20.pdf.* Accessed 09.07.2015.
18. 23. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2010 Update. Available at: *http://www.goldcopd.org/Guidelines/guideline-2010-gold-report.html.* Accessed 09.07.2015.
19. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PloS Med 2006; 3: e442.
20. Minov J, Karadzinska-Bislimovska J, Vasilevska K, Risteska-Kuc S, Stoleski S. Exposure to environmental tobacco smoke in the workplace in Macedonia: Where are we now? Arh Hig Rada Toksikol 2008; 59: 103-109.
21. Minov J, Karadzinska-Bislimovska J, Vasilevska K, Nelovska Z, Risteska-Kuc S, Stoleski S, Mijakoski D. Smoking among Macedonian workers five years after the anti-smoking campaign. Arh Hig Rada Toksikol 2012; 63: 207-213.
22. Becklake RM. Grain dust and lung health: Not just a nuisance dust. Can Respir J 2007; 14 (7): 423-425.
23. Warren O, Cherniack RM, Tse KS. Hypersensitivity reactions to grain dust. J Allergy Clin Immunol 1974; 53: 139-149.
24. Dosman JA, Cotton DJ, Graham BJ, et al. Chronic bronchitis and decreased forced respiratory flow rates in lifetime nonsmoking grain workers. Am Rev Respir Dis 1980; 121: 11-16.
25. Dales RE, Ernst P, Blanchet Y, Bourbeau J. Does seasonal employment in grain elevatorsincrease nonspecific airways responsiveness? J Occup Med 1988; 30: 613-616.
26. Huy T, De Schipper K, Chan-Yeung M, Kennedy SM. Grain dust and lung function. Dose-response relationships. Am Rev Respir Dis 1991; 144: 1314-1321.
27. Chan-Yeung M, Dimich-Ward H, Enarson DA, Kennedy SM. Five cross-sectional studies of grain elevator workers. Am J Epidemiol 1992; 136: 1269-1279.
28. Post W, Heederik D, Houba R. Decline in lung function related to exposure and selection processes among workers in the grain processing and animal feed industry. Occup Environ Med 1998; 55 (5): 349-355.
29. Mohammadien HA, Hussein MT, El-Sokkary RT. Effects of exposure to flour dust on respiratory symptoms and pulmonary function of mill workers. Egyptian Journal of Chest Diseases and Tuberculosis 2013; 62: 745-753.
30. Bachmann M, Myers JE. Grain dust and respiratory health in South African milling workers. Br J Ind Med 1991; 48 (10): 656-662.

The Turkish Journal of Occupational / Environmental Medicine and Safety

Vol:1, No: 3 Web: http://www.turjoem.com ISSN : 2149-4711

31. Minov J, Karadzinska-Bislimovska J, Vasilevska K, et al. Chronic obstructive pulmonary disease in never-smoking bricklayers. Maced J Med Sci 2013. http://dx.doi.org/10.3889/MJMS.1857-5773.2013.0329.

Minov J, Karadzinska-Bislimovska J, Tutkun E, et al. Chronic obstructive pulmonary disease in never-smoking female workers exposed to cotton dust. Maced J Med Sci 2014. http://dx.doi.org/10.3889/MJMS.1857-5773.2014.0386.