

# Respiratory Symptoms and Ventilatory Function in Never-Smoking Males Working in Dusty Occupations

Marina Danilova<sup>1\*</sup>, Saso Stoleski<sup>2</sup>, Dragan Mijakoski<sup>2</sup>

<sup>1</sup>Faculty of Medical Sciences, University „Goce Delchev“, Shtip, Republic of Macedonia; <sup>2</sup>Institute for Occupational Health of Republic of Macedonia, WHO Collaborating Center and GA2LEN Collaborating Center, Skopje, Republic of Macedonia

## Abstract

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**\*Correspondence:** Marina Danilova. „Krstе Misirkov“ No.10-A, P.O 201, Stip - 2000, Republic of Macedonia. cell phone +389 75 514 519. Fax: +389 32 390 700. E-mail: marina.danilova@ugd.edu.mk

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**AIM:** To assess the effect of occupational exposure on respiratory symptoms and ventilatory capacity in never-smoking male workers exposed to mineral or organic dusts.

**MATERIAL AND METHODS:** We performed a cross-sectional study including 138 never-smoking male workers exposed to mineral or organic dust (34 construction workers, 32 furniture manufacturers, 37 agricultural workers, and 35 bakers) and 35 unexposed controls (office workers). Evaluation of all study subjects included completion of a questionnaire and spirometric measurements.

**RESULTS:** The prevalence of the overall respiratory symptoms in the last 12 months was higher in dusty occupation workers than its prevalence in office workers. Statistically significant difference was found between the prevalence of cough in construction workers, agricultural workers and bakers, as well as between the prevalence of phlegm in construction workers, furniture manufacturers and agricultural workers as compared to its prevalence in office workers. The mean values of spirometric parameters were lower in all groups of exposed workers as compared to their mean values in office workers with statistical significance for all measured parameters in construction workers and furniture manufacturers, as well as for small airways indices in agricultural workers and bakers.

**CONCLUSION:** Our findings indicate significant effect of occupational exposure on respiratory symptoms and ventilatory capacity impairment in workers exposed to mineral or organic dusts.

## Introduction

Despite the number of workers employed in dusty occupations, especially in the developed countries, is on the decline, million workers are exposed to different types of mineral (inorganic) or organic dust. For example, it was established that at the end of the last century over two million workers are exposed to wood dust around the world [1]. Overall last decades several papers have described the relationship between occupational exposure, smoking and respiratory impairment [2-6]. It has been suggested that the effects of exposure to dust were of a different kind and probably less harmful than those of smoking [7, 8]. This topic still remains controversial.

The aim of the present study is to assess the effect of occupational exposure on respiratory

symptoms and lung function in never-smoking male workers exposed to mineral and organic dusts.

## Methods

### *Study design and setting*

A cross-sectional study was carried out at the Institute for Occupational Health of Republic of Macedonia, Skopje - WHO Collaborating Center for Occupational Health and GA<sup>2</sup>LEN Collaborating Center in the period November 2013-May 2014. Prevalence of chronic respiratory symptoms and mean values of spirometric parameters were compared between groups of never-smoking workers exposed to mineral and organic dusts and a group of never-smoking administrative workers.

The study protocol was approved by the ethics committee of the institution and each subject gave an informed consent before entering the study.

### Subjects

We examined 138 never-smoking male workers exposed to mineral or organic dust: construction workers, furniture manufacturers, bakers, and agricultural workers. All study subjects were informed about the study and their written consent was obtained.

The group of construction workers consisted of 34 males employed as bricklayers. The common materials of their work include brick, concrete, stone, whitewash, granite, travertine, marble, man-made mineral fibres etc., i.e. they were occupationally exposed predominantly to cement dust.

The group of furniture manufacturers consisted of 32 males occupationally exposed to wood dust, as well as to vapors from adhesives, paints and other chemical agents.

The agricultural workers included 37 males employed in vegetable cultivating (planting, digging, irrigation, etc.), i.e. their occupational exposure include both mineral and organic dusts.

The group of bakers included 35 males employed at industrial bakery. Their occupational exposure included flour dust, as well as substances added during bread making process (alpha-amylase, bakers' yeast, etc.).

In addition, a group of 35 male office (administrative) workers matched to exposed workers by age and smoking status were studied as a control.

In either group there were no subjects with chronic respiratory disease diagnosed by physician (i.e. asthma, COPD, chronic bronchitis, bronchiectasis, etc.), neither subject treated with bronchodilators and/or corticosteroids. In either group also there were no subjects in whom spirometry testing was contraindicated (9, 10).

### 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, family history of asthma or COPD (taking into account the first-degree relatives), 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 [11, 12].

Never-smokers were defined according to the World Health Organization (WHO) Guidelines for Controlling and Monitoring the Tobacco Epidemic as the people who have never smoked at all or have never been daily smokers and have smoked less than 100 cigarettes in their life time [13].

### Spirometry

Spirometry, including measures of forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), FEV<sub>1</sub>/FVC ratio, and maximal expiratory flow at 50%, 25%, and 25-75% of FVC (MEF<sub>50</sub>, MEF<sub>25</sub>, and MEF<sub>25-75</sub>, 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<sub>1</sub> 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 Respiratory Society (ERS) and American Thoracic Society (ATS) (4A, 5A).

### Statistical analysis

Continuous variables were expressed as mean values with standard deviation (SD), and the nominal variables as numbers and percentages. Analyses of the data involved testing the differences in prevalence and comparison of the means. Chi-square test (or Fisher's exact test where appropriate) was used for testing difference in the prevalence of the respiratory symptoms in the last 12 months. Comparison of spirometric measurements was performed by independent-samples *T*-test. The association between mean value of FEV<sub>1</sub> (less or more than 75% of predicted value) and duration of exposure (less or more than 15 years) was tested by chi-square test. A *P*-value less than 0.05 was considered as statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows.

## Results

Characteristics of the subjects enrolled in the study are given in Table 1.

We found higher prevalence of the overall respiratory symptoms in the last 12 months in the groups of the workers exposed to mineral or organic dust than in the group of office workers but the statistical significance of the difference was not reached. In addition, the prevalence of the overall

**Table 1: Demographics of the study subjects.**

Variable	Construction workers (n = 34)	Furniture manufacturers (n = 32)	Agricultural workers (n = 37)	Bakers (n = 35)	Office workers (n = 35)
Mean age (yrs)	41.3 ± 9.4	43.9 ± 6.7	41.7 ± 5.7	44.1 ± 9.1	42.4 ± 7.1
BMI (kg/m <sup>2</sup> )	24.4 ± 2.4	25.7 ± 3.9	25.1 ± 2.3	26.3 ± 3.4	25.3 ± 3.1
Mean duration of employment at the actual workplace (yrs)	14.6 ± 7.8	13.4 ± 7.2	14.1 ± 6.4	15.2 ± 4.9	15.8 ± 4.6
Less than 15 yrs	19 (55.9%)	18 (56.3%)	21 (56.8%)	17 (48.5%)	16 (45.7%)
More than 15 yrs	15 (44.1%)	14 (43.7%)	16 (43.2%)	18 (51.3%)	19 (54.3%)
Family history of asthma/COPD	4 (11.8%)	3 (9.4%)	4 (10.8%)	4 (11.4%)	3 (8.6%)
Accompanying diseases					
Arterial hypertension	3 (8.8%)	3 (9.4%)	4 (10.8%)	3 (8.6%)	4 (11.4%)
Diabetes mellitus type 2	2 (5.9%)	1 (3.1%)	2 (5.4%)	2 (5.7%)	3 (8.5%)
Peptic ulcer	2 (5.9%)	2 (6.2%)	3 (5.4%)	3 (8.5%)	2 (5.7%)

Numerical data are expressed as mean value with standard deviation; the frequencies as number and percentage of examinees with certain variable. Yrs: years; kg: kilogram; m: meter; COPD: chronic obstructive pulmonary disease.

respiratory symptoms in the last 12 months in the exposed workers from different occupation groups was similar (Figure 1).

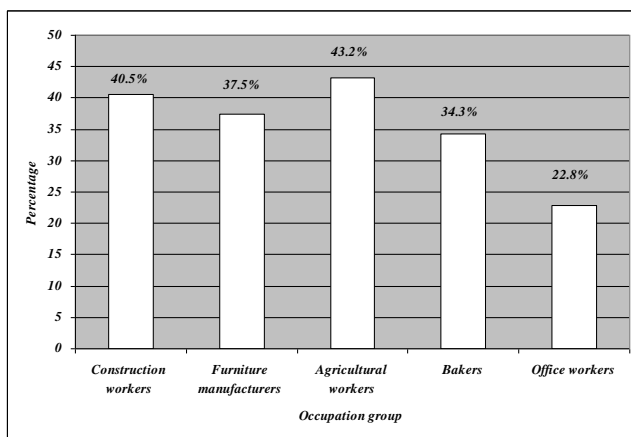


Figure 1: Prevalence of the overall respiratory symptoms in the last 12 months in examined groups.

The prevalence of all particular respiratory symptoms in the last 12 months was also higher in the groups of exposed workers than in the group of office workers. Statistically significant difference was found between the prevalence of cough in construction workers, agricultural workers and bakers and its prevalence in office workers ( $P = 0.029$ ;  $P = 0.041$ ; and  $P = 0.038$ ; respectively), as well as between the prevalence of phlegm in construction workers, furniture manufacturers and agricultural workers and its prevalence in office workers ( $P = 0.031$ ;  $P = 0.043$ ; and  $P = 0.039$ ; respectively) (Table 2).

**Table 2: Prevalence of particular respiratory symptoms in the last 12 months in examined groups.**

Respiratory symptom in the last 12 months	Construction workers (n = 34)	Furniture manufacturers (n = 32)	Agricultural workers (n = 37)	Bakers (n = 35)	Office workers (n = 35)
Cough	9 (26.5%)	8 (25.0%)	11 (29.7%)	9 (25.7%)	4 (11.4%)
Phlegm	5 (14.7%)	4 (12.5%)	5 (13.5%)	4 (11.4%)	2 (5.7%)
Dyspnea	4 (11.7%)	3 (9.3%)	4 (10.8%)	4 (11.4%)	3 (8.5%)
Wheezing	3 (8.8%)	3 (9.3%)	4 (10.8%)	3 (8.5%)	2 (5.7%)
Chest tightness	4 (11.7%)	4 (12.5%)	5 (13.5%)	4 (11.4%)	3 (8.5%)

Data are expressed as number and percentage of examinees with certain variable.

The mean values of spirometric parameters were lower in all groups of exposed workers as compared to their mean values in office workers. Statistical significance was obtained for all measured parameters in construction workers and furniture manufacturers, as well as for small airways indices in agricultural workers and bakers. As with the prevalence of respiratory symptoms in the last 12 months, the mean values of measured spirometric parameters in the exposed workers from different occupation groups was similar (Table 3).

**Table 3: Mean values of spirometric parameters in examined groups.**

Spirometric parameter	Construction workers (n = 34)	Furniture manufacturers (n = 32)	Agricultural workers (n = 37)	Bakers (n = 35)	Office workers (n = 35)
FVC (%pred)	87.2 ± 12.2	86.4 ± 11.9	88.1 ± 10.6	89.9 ± 9.4	94.1 ± 9.1
FEV <sub>1</sub> (%pred)	73.1 ± 7.9	72.2 ± 5.6	71.4 ± 9.1	74.0 ± 8.6	82.9 ± 8.7
FEV <sub>1</sub> /FVC%	0.77 ± 0.03	0.78 ± 0.04	0.81 ± 0.06	0.82 ± 0.07	0.83 ± 0.06
MEF <sub>50</sub> (%pred)	55.9 ± 8.8	53.9 ± 14.6	57.7 ± 11.2	55.4 ± 13.2	70.7 ± 6.9
MEF <sub>25</sub> (%pred)	39.1 ± 8.2	35.0 ± 11.2	47.0 ± 7.9	47.8 ± 11.9	64.3 ± 8.7
MEF <sub>25-75</sub> (%pred)	74.8 ± 12.6	70.3 ± 15.8	76.7 ± 11.9	73.7 ± 14.4	89.5 ± 10.3

Data are expressed as mean value with standard deviation. FVC: forced vital capacity; FEV<sub>1</sub>: forced expiratory volume in one second; MEF<sub>50</sub>, MEF<sub>25</sub>, MEF<sub>25-75</sub>: maximal expiratory flow at 50%, 25% and 25-75% of FVC, respectively; % pred: % of predicted value.

We found significantly higher prevalence of workers with mean value of FEV<sub>1</sub> less than 75% of predicted value and duration of occupational exposure longer than 15 years than its prevalence among workers with shorter duration of exposure in the groups of construction workers ( $P = 0.033$ ), agricultural workers ( $P = 0.037$ ) and bakers ( $P = 0.043$ ), while among furniture workers this prevalence just missed statistical significance ( $P = 0.062$ ). This association in office workers was statistically non-significant ( $P = 0.114$ ).

## Discussion

Many studies report that occupational exposure to dusts, vapours, gases, and fumes may cause respiratory impairment of different type and severity. In addition, there is evidence that occupational exposure to mineral or organic dust may lead to respiratory impairment independent of any effect due to smoking and separate from other effects of exposure such as pneumoconiosis, asthma, COPD or hypersensitivity pneumonitis [14-17]. In the present study we compared the prevalence of respiratory symptoms in the last 12 months and values of the spirometric measurements in never-smoking male workers exposed to different types of mineral or organic dusts (construction workers, furniture manufacturers, agricultural workers, and bakers) and unexposed controls (office workers).

All occupation groups consisted of subjects with similar demographic characteristics. The workers from four occupation groups (construction workers, furniture manufacturers, agricultural workers, and bakers) were predominantly exposed to mineral or

organic dust, as well as to other substances related to processing of certain occupation.

We found higher prevalence of the overall respiratory symptoms in the last 12 months in all occupation groups exposed to mineral or organic dust than its prevalence in office workers. Statistically significant difference was found between the prevalence of cough in construction workers, agricultural workers and bakers, as well as between the prevalence of phlegm in construction workers, furniture manufacturers and agricultural workers as compared to its prevalence in office workers. Similar results were reported by several studies that investigated respiratory effects of occupational exposures to various dust types. Nguyen et al. [18] in a population-based study performed in Vietnam indicated that occupational exposures to dust caused increase in chronic respiratory symptoms independent of the effect of cigarette smoking. The study among farmers in France indicated synergetic effect of occupational exposure and smoking, especially for cough and phlegm [19]. An excess of acute and chronic respiratory symptoms in workers exposed to similar occupational exposure is reported in several studies [20-22]. Pramanik & Chaudhury [23] reported that more than a half of carpenters working in furniture industries in West Bengal suffered from one or several respiratory symptoms. Abrons et al. [24] reported significantly higher prevalence of dyspnea among cement workers than other workers not exposed to dust. In addition, higher prevalence of respiratory symptoms in comparison with administrative workers are also found in workers exposed to another dust types. In the study that investigated respiratory effects of occupational exposure to cotton dust, Minov et al. [25] registered higher prevalence of overall respiratory symptoms in the last 12 months in never-smoking female cotton spinners than in never-smoking female office workers with statistically significant difference for phlegm and dyspnea.

The mean values of spirometric parameters were lower in all occupation groups exposed to mineral or organic dust as compared to its mean value in unexposed controls. Statistical significance was obtained for all measured parameters in construction workers and furniture manufacturers, as well as for small airways indices in agricultural workers and bakers. The association between the mean value of FEV<sub>1</sub> and duration of occupational exposure followed dose-response pattern in all groups exposed to mineral or organic dust. Similar findings were reported by several studies which investigated lung function parameters among workers from dusty occupations. Significantly lower mean values of FVC, FEV<sub>1</sub>, and FEV<sub>1</sub>/FVC was found in the workers exposed to cement dust as compared to non-exposed controls in the study conducted by Al-Neaimi et al [26]. Similarly, Bosan & Okpapi [27] reported significant reduction of FVC, FEV<sub>1</sub> and peak expiratory flow rate (PEFR) among wood workers in the Savannah Belt in

Northern Nigeria. Dosman et al. [28] investigating the effect of the occupational exposure on respiratory symptoms and ventilatory function in cereal grain farmers in Denmark reported significantly lower mean values of FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, and MEF parameters in these workers as compared to their values in unexposed controls. On the contrary, in a study investigating exercise-induced respiratory symptoms and exercise-induced bronchoconstriction in industrial bakers, Minov et al. [29] registered lower mean values of all measured spirometric parameters (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, MEF<sub>50</sub>, MEF<sub>25</sub>, and MEF<sub>25-75</sub>) as compared to their mean values in office workers but statistically significant difference was not found for any parameter.

The present study has some limitations. First, relatively small number of the subjects in the examined occupation groups could have certain implications on the data obtained and its interpretation. Second, environmental measurements were not performed, so we could not document the effect of the type and the level of exposure on respiratory symptoms and ventilatory capacity impairment. Third, the impact of healthy workers' effect on the data obtained could not be excluded. The strength of the study is assessment of respiratory effects of never-smoking workers from several occupations exposed to mineral or organic dusts.

In conclusion, in a cross-sectional study aimed at assessment of the respiratory effects of occupational exposure on construction workers, furniture manufacturers, agricultural workers and bakers we found higher prevalence of respiratory symptoms in the last 12 months in all exposed groups than in office workers, as well as lower values of spirometric parameters than in office workers. Our data indicate the need of improvement of all types of preventive measures in order to protect the further respiratory impairment of exposed workers.

## Authors Participations

DM participated in the study design, writing the protocol, data collection, managing the analyses of the study, and writing all versions of the manuscript. SS and MD participated in the study design, data collection, managing the analyses of the study, as well as writing all versions of the manuscript.

## References

1. Wood Dust and Formaldehyde. WHO 1997. Available from: <http://monographs.iarc.fr/ENG/Monographs/vol62/volume62.pdf> (Accessed 07.07.2014).
2. Higgins ITT, Cochrane AL, Gilson JC, Wood CH. Population studies of chronic respiratory disease: a comparison of miners, foundry workers, and others in Staveley, Derbyshire. *Br J Ind Med.* 1959; 16: 255-268.
3. Lebowitz MD. Occupational exposures in relation to

- simptomatology and lung function in a community population. *Environ Res.* 1977; 14: 59-67.
4. Kauffmann F, Drouet D, Lellouch J, Brille D. Occupational exposure and 12-year spirometric changes among Paris area workers. *Br J Ind Med.* 1982; 39: 221-332.
  5. Korn RJ, Dockery DW, Speizer FE, Ware JH, Ferris BG Jr. Occupational exposures and chronic respiratory symptoms. A population-based study. *Am Rev Respir Dis.* 1987; 136: 298-304.
  6. Blanc PD, Iribarren C, Trupin L, Earnest G, Katz PP, Balmes J, Sidney S, Eisner MD. Occupational exposures and the risk of COPD: dusty trades revisited. *Thorax.* 2009; 64: 6-12.
  7. Morgan WKC. Industrial bronchitis. *Br J Ind Med.* 1978; 35: 285-291.
  8. Vestbo J, Knudsen KM, Rasmussen FV. The effect of smoking and occupation on changes in respiratory symptoms in middle-aged Danish men. *Eur Respir J.* 1990; 3: 880-885.
  9. Spirometry Guide: 2010 Update. Available at: <http://www.goldcopd.org/uploads/users>. (Accessed 07.07.2014).
  10. 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.
  11. 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.
  12. 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.
  13. World Health Organization. Guidelines for controlling and monitoring the tobacco epidemic. Geneva: WHO, 1998.
  14. Beclacke MR. Chronic airflow limitation: its relationship to work in dust occupations. *Chest.* 1985; 88: 608-617.
  15. Beclacke MR. Relationship of acute obstructive airway change to chronic (field) obstruction. *Thorax.* 1995; 50 (1): S16-S52.
  16. Dimich-Ward H, Kennedy SM, Chan-Yeung M. Occupational exposures and chronic airflow limitation. *Can Respir J.* 1996; 3: 133-140.
  17. Minov J, Karadzinska-Bislimovska J, Risteska-Kuc S, Stoleski S. Chronic respiratory symptoms and ventilatory function in workers exposed to tea dust: effect of duration of exposure and smoking. *Facta Universitatis.* 2005; 12 (1): 37-43.
  18. Nguyen MS, Nguyen JH, Nguyen VH, Dinh HT, Le VT, Nguyen TC, Hoang MT, Phung HD, Dang DT. Occupational exposure and chronic respiratory symptoms – a population-based study in Vietnam. *Industrial Health.* 1997; 35 (2): 271-277.
  19. Dalphin JC, Dubiez A, Monnet E, Gora D, Westeel V, Pernet D, Polio JC, Gibey R, Laplante JJ, Depierre A. Prevalence of asthma and respiratory symptoms in dairy farmers in the French province of the Doubs. *Am J Respir CRIT Care Med.* 1998; 158: 1493-1498.
  20. Zuskin E, Mustajbegovic J, Schachter EN, Kern J, Doko-Jelinic J, Godnic-Cvar J. Respiratory findings in workers employed in brick-manufacturing industry. *J Occup Environ Med.* 1998; 40: 814-820.
  21. Meijer E, Krombout H, Heederik D. Respiratory effects of exposure to low levels of concrete dust containing crystalline silica. *AM J Ind Med.* 2001; 40: 133-140.
  22. Barber CM, Fishwick D. Chronic cough – occupational considerations. *Chron Respir Dis.* 2008; 5 (4): 211-221.
  23. Pramanik P, Chaudhury A. Impact of occupational exposure to wood dust on pulmonary health of carpenters in small scale furniture industries in West Bengal. *DHR-IJBLS.* 2013; 4 (3): 204-211.
  24. Abrons HL, Peterson MR, Sanderson WT, Engelberg AL, Harber P. Symptoms, ventilatory function, and environmental exposures in Portland cement workers. *Br J Ind Med.* 1988; 45: 368-375.
  25. Minov J, Karadzinska-Bislimovska J, Tutkun E, Vasilevska K, Risteska-Kuc S, Stoleski S, Mijakoski D. Chronic obstructive pulmonary disease in never-smoking female workers exposed to cotton dust. *Maced J Med Sci.* 2014; 7(2):320-326.
  26. Al-NeaimiYI, Gomes J, Lloyd OL. Respiratory illnesses and ventilatory function among workers at a cement factory in a rapidly developing country. *Occup Med.* 2001; 51: 367-373.
  27. Bosan IB, Okpapi JU. Respiratory symptoms and ventilatory function impairment among wood workers in the Savannah Belt of Northern Nigeria. *Annals of African Medicine.* 2004; 3 (1): 22-27.
  28. Dosman JA, Graham BL, Hall D, van Loon P, Bhasin P, Froh F. Respiratory symptoms and pulmonary function in farmers. *J Occup Med.* 1987; 29: 38-42.
  29. Minov J, Karadzinska-Bislimovska J, Vasilevska K, Stoleski S, Mijakoski D. Exercise-related respiratory symptoms and exercise-induced bronchoconstriction in industrial bakers. *Arch Environ Occup Health.* 2013; 68 (4): 235-242.