Specific work activities and exposure to respiratory hazards - predictors of lung function impairment among crop farmers

Sasho Stoleski*, Jordan Minov, Dragan Mijakoski, Aneta Atanasovska, Dragana Bislomovska, Jovanka Karadzinska-Bislomovska

Center for Respiratory Functional Diagnostics, Institute for Occupational Health, World Health Organization Collaborating Center and Ga2len Collaborating Center, Skopje, Republic of Macedonia

Abstract

OBJECTIVE: The objective of the study was to evaluate the specific work activities and occupational exposure to respiratory hazards as predictors of chronic respiratory symptoms development, lung function decline, and respiratory health impairment among crop farmers.

METHODS: A cross-sectional survey was performed, including 87 crop farmers (mean age: 53.4 ± 7.8 years; and mean exposure duration: 22.9 ± 7.8 years) and 80 office workers as a control group (mean age: 52.7 ± 8.2 years) matched for age, smoking habits, and socioeconomic status. Subjects were evaluated by a questionnaire on respiratory symptoms in the past 12 months and spirometry testing.

RESULTS: Crop farmers had a significantly higher prevalence of cough (41.4), phlegm (28.7%), and dyspnea (21.8%), than controls (p < 0.05). All mean baseline spirometric parameters were lower in crop farmers, but statistical significance was confirmed only for MEF21 (p = 0.003, p = 0.000, and p = 0.001, respectively). Most of the respiratory symptoms were significantly associated with common work activities of crop farmers and all-day exposure to certain respiratory hazards. Age, exposure duration, and their combined effect with smoking habit had a significant effect on forced expiratory volume in one second FEV1, and FEV1/forced vital capacity.

CONCLUSION: The results confirm that occupational exposure among crop farmers is associated with higher prevalence of respiratory symptoms and lung function decline and, together with specific workflow activities, may not only be a predictors of respiratory health impairment, but also a key tool in the creation of preventive strategies.

Introduction

Respiratory hazards are one of the most common occupational hazards in agriculture and can cause different types of respiratory disorders among exposed workers [1]. Farmers are exposed to various inhalation agents: Inorganic soil dust, organic dust containing microorganisms, mycotoxins and allergens, decomposition gases, pesticides, and others. This exposure most often occurs during soil cultivation, harvesting, processing, and storage of grain and other plants, breeding animals, etc. [2].

Exposure to organic dust varies qualitatively and quantitatively, depending on the types of agricultural activities, namely, the grain dust contains molds, spores, mycotoxins, bacteria and their components, excreta, microbes, insects, and animal products. In other cases, grain dust may contain particles of cotton, paper, flour, tobacco, and other dust [3].

Chronic, primarily obstructive pulmonary diseases are nowadays a major clinical and public health problem for agricultural workers, and especially crop farmers. Numerous studies conducted in the last few decades show a significantly higher risk for respiratory morbidity and mortality among crop farmers, demonstrating the link between respiratory hazards in agriculture and not only the development of chronic respiratory symptoms but also the development of chronic respiratory [1].

Breathing problems associated with exposure to dust in farming were first noted and described by Ramazzini in 1713 [4]. In recent decades, chronic respiratory symptoms and diseases have been well known among farmers [5], cattle breeders [6], and pig workers [7], although the magnitude of the problem has not yet been sufficiently assessed [8]. Chronic lung disease in crop farmers can be caused by a wide range of respiratory harmful agents [9], [10].

All of these harmful substances present in the working environment of crop farmers can cause or aggravate: Organic dust toxic syndrome, chronic bronchitis, allergic and non-allergic asthma, asthma-like syndrome, chronic obstructive pulmonary disease
(COPD), chemical or hypersensitive pneumonitis [11], [12], allergic and non-allergic rhinitis, etc [13].

Data obtained from our previous surveys in this field [14], [15], show that the most common work activities among crop farmers include fieldwork, planting, digging, watering, mechanization and pesticide use, irrigation, harvesting, and cleaning workplaces. During the working process, they are exposed to adverse microclimate conditions, inorganic and organic dust, chemical hazards and pesticides, contact with plants, etc.

Despite the fact that these hazards and dangers are well documented [16], there is little information on the modes and intensity of exposure. Changes in the workflow and farming practices over the last few decades have contributed to a dramatic increase in the concentration of dust and chemical hazards in ambient air [17]. In general, farms are larger, cereal production is increased, and dust, gases, and microorganisms are in high concentrations and represent significant respiratory hazards that play an important role in the development and progression of chronic respiratory diseases [18].

Many epidemiological and clinical studies report a higher prevalence of chronic respiratory symptoms and lung function impairments among agricultural workers compared to other occupations. The frequency of respiratory symptoms depends on the type of farming activity, but mostly on the intensity and length of exposure to organic dust. Research indicates a lower frequency of respiratory symptoms among farmers whose main activity is in growing crops, compared to those engaged in livestock breeding [19].

There is a wealth of data showing that occupational exposure in crop farming may be associated with chronic lung diseases. Dust from cereals and fodder, fertilizer gases, disinfectant vapors, as well as endotoxins and spores from microorganisms are key elements of occupational exposure in crop farmers and identified as likely promoters of airway inflammation [20].

In the present study, we have evaluated specific work activities and occupational exposure to respiratory hazards as predictors of chronic respiratory symptoms development, lung function decline, and respiratory health impairment among crop farmers.

Subjects and Methods

Study design and setting

The research team from the Institute for Occupational Health, Skopje – World Health Organization (WHO) Collaborating Center, and GA2LEN Collaborating Center performed a cross-sectional survey in the Center for Respiratory Functional Diagnostics within in the period from August 2018 to February 2019.

Study sample

To be representative, the study sample was calculated by the software program PEPI 4.04, with 95% confidence level and confidence interval (CI) ±5.

Aiming to fulfill the requested sample size, and keeping in mind possible selection and response bias, we have taken a representative sample of 87 crop farmers and 80 matched office controls in a large scale agricultural enterprise.

Subjects

Our research team has examined, 87 subjects (mean age=53.4 ± 7.8) employed as crop farmers (mean duration of exposure 22.9 ± 7.8). They were engaged in crop farming with main activities composed of cultivating and harvesting crops, planting, digging, use of mechanized equipment, irrigation, cleaning premises, and pesticide handling. Crop farmers were exposed to various respiratory agents, including dust, inappropriate climate and temperature amplitudes, fumes, vapors, and pesticides. Inclusion criteria for examined group (EG) employed subjects with age range 18–64 years involved in dairy farming and exposed to at least one occupational respiratory hazard (dust, gases, fumes, and vapors).

Exclusion criteria for EG subjects younger than 18 or older than 64 years, and subjects not engaged in crop farming were excluded from the study. To avoid selection bias and results’ deviations, the study did not include subjects with exposure to respiratory hazards other than crop farming.

Depending on the exposure duration, the examined subjects were divided into two subgroups: Exposed less or more than 20 years.

Furthermore, similar group of 80 office workers (mean age = 52.7 ± 8.2) matched for age, duration of employment, daily smoking, and socioeconomic status was studied as a control group (CG), with no data on occupational exposure to respiratory hazards.

Subjects in both groups, diagnosed by a physician to have some chronic respiratory disorder (asthma, COPD, bronchiectasis, sarcoidosis, etc.), or treated with bronchodilators and/or corticosteroids were excluded from the study. Furthermore, both groups did not comprise any subjects in whom spirometry testing was contraindicated.

The Institute Ethics Committee has approved our study protocol, whereas each examined subject was informed and gave written consent before proceeding any involvement in the survey.
**Questionnaire**

All study subjects were interviewed by physician and completed the standardized questionnaire, including questions on work history, respiratory symptoms in the past 12 months, and smoking habits.

Chronic respiratory symptoms in the past 12 months (cough, phlegm, dyspnea, wheezing, and chest tightness) were obtained using the European Community for Coal and Steel questionnaire (ECCS-87), and the European Community Respiratory Health Survey questionnaire [21], [22].

Smoking status was classified according to the WHO guidelines on its’ definitions [23]. Daily smoker was defined as a subject who smoked at the time of the field survey at least once a day, except on days of religious fasting. Among daily smokers, lifetime cigarette smoking and daily mean of cigarettes smoked were also assessed. Pack-years smoked were calculated according to the actual recommendations [24].

Ex-smoker was defined as a formerly daily smoker, no longer smokes.

Passive smoking or exposure to environmental tobacco smoke was defined as the exposure of a person to tobacco combustion products from smoking by others [25].

**Baseline spirometry**

All study subjects underwent spirometry testing, performed by spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany), measuring forced vital capacity (FVC), forced expiratory volume in one second (FEV\(_1\)), FEV\(_1\)/FVC ratio, and maximal expiratory flow at 50%, 75%, and 25–75% of FVC (MEF\(_{50%}\), MEF\(_{75%}\) and MEF\(_{25-75%}\) respectively), by recording the best result from three measurements of the values of FEV\(_1\) within 5% of each other. The results were expressed as percentages of the predicted values according to the European Community of Coal and Steel norms. The spirometry results were given as percents of their predicted values due to the current European Respiratory Society and American Thoracic Society recommendations including reproducibility and acceptability [26].

**Statistical analysis**

The obtained data were analyzed using Statistica for Windows version 7. Continuous variables were expressed as mean values with standard deviation and categorical variables as numbers and percentages. The Chi-square test (or Fisher’s exact test) was used for testing differences in the prevalence of respiratory symptoms, while the comparison of spirometric measurements was performed by independent-samples t-test. p < 0.05 was considered statistically significant. Logistic and multiple linear regression analysis was used to assess the risk for the development of chronic respiratory symptoms related to workflow characteristics in crop farmers and lung function impairment, adjusted for age, exposure duration, and smoking habit. Study variables were checked for normality by Kolmogorov–Smirnov and Shapiro–Wilk’s W test.

**Results**

An overview of the overall and demographic characteristics of the study subjects is shown in Table 1.

| Table 1: Demographics of the study subjects |
| Variable | Crop farmers (n=87) | Office workers (n=80) |
|----------|---------------------|----------------------|
| Gender/MI ratio | 3.6 | 2.7 |
| Age range (years) | 20–63 | 21–64 |
| Age (years) | 53.4 ± 7.8 | 52.7 ± 8.2 |
| BMI (kg/m\(^2\)) | 25.6 ± 3.5 | 26.2 ± 3.7 |
| Duration of employment (years) | 28.2 ± 9.9 | 25.3 ± 9.8 |
| Duration of exposure | 22.0 ± 7.8 | / |
| Daily smokers (%) | 45 (51.7) | 39 (48.7) |
| Life-time smoking (years) | 19.7 ± 8.1 | 19.2 ± 7.8 |
| Cigarettes/day | 15.4 ± 7.3 | 14.8 ± 7.2 |
| Pack-years smoked | 13.1 ± 4.8 | 12.9 ± 4.9 |
| Ex-smokers (%) | 12 (13.8) | 12 (15) |
| Passive smokers (%) | 11 (12.6) | 8 (16) |

Numerical data are expressed as mean value with standard deviations; frequencies as number and percentage of study subjects with certain variable. BMI: Body mass index; kg: Kilogram; m: meter, OR: Odds ratio, CI: Confidence interval.

Neither diagnose of any chronic respiratory non-occupational disease (sarcoidosis, tuberculosis) established before the study nor treatment with oral corticosteroids, bronchodilators, antihistamines, or any other medications that could potentially influence the functional and clinical findings were reported by the study subjects.

The frequency of chronic respiratory symptoms in the past 12 months is higher in crop farmers compared to office controls, with a significant difference for cough, cough with phlegm, and dyspnea (Table 2). The association of respiratory symptoms and exposure duration among dairy farmers is shown in Table 2.

| Table 2: Prevalence of respiratory symptoms in the past 12 months in both examined groups and prevalence of respiratory symptoms in the past 12 months in crop farmers with the duration of workplace exposure more and <20 years |
| Respiratory symptoms in the past 12 months | Crop farmers (n=87) | Office workers (n=80) | OR (95% CI) | p-value* |
|----------|---------------------|----------------------|-------------|----------|
| Any respiratory symptom | 38 (43.7) | 23 (21.2) | 1.81 (0.91–3.61) | 0.067 |
| Cough | 36 (41.4) | 17 (24.3) | 2.72 (1.30–5.75) | 0.003 |
| Phlegm | 25 (28.7) | 12 (15) | 2.28 (1.00–5.31) | 0.032 |
| Dyspnea | 19 (21.8) | 8 (10) | 2.51 (0.96–6.75) | 0.037 |
| Wheezing | 14 (16.1) | 8 (10) | 1.73 (0.63–4.83) | 0.244 |
| Chest tightness | 9 (10.3) | 6 (7.5) | 1.42 (0.51–3.70) | 0.520 |

Crop farmers

| Respiratory symptoms in the past 12 months | Exposed >20 years (n=66) (%) | Exposed ≤20 years (n=21) (%) | OR (95% CI) | p-value* |
|----------|-----------------------------|-----------------------------|-------------|----------|
| Any respiratory symptom | 33 (50) | 5 (23.8) | 3.20 (0.95–11.41) | 0.035 |
| Cough | 32 (48.5) | 4 (19.1) | 4.00 (1.10–15.87) | 0.017 |
| Phlegm | 23 (34.8) | 2 (9.5) | 6.44 (1.28–45.62) | 0.008 |
| Dyspnea | 17 (25.7) | 2 (9.5) | 3.30 (0.63–22.84) | 0.141 |
| Wheezing | 12 (18.2) | 2 (9.5) | 2.59 (0.47–18.59) | 0.326 |
| Chest tightness | 7 (10.6) | 2 (9.5) | 1.13 (0.19–6.63) | 0.887 |

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. OR: Odds ratio, CI: Confidence interval.
The risk for the development of chronic respiratory symptoms is about three-fold higher among crop farmers exposed more than 20 years compared to those with shorter job exposure (odds ratio [OR] = 3.20 [0.95–11.41] CI 95%).

Crop farmers have lower mean values of spirometric parameters compared to controls, but being significantly only for MEF_{25}%, MEF_{50}%, and MEF_{75%} (Table 3).

**Table 3: Mean values of spirometric parameters in examined groups and mean values of spirometric parameters in crop farmers with the duration of workplace exposure more and <20 years**

| Spirometric parameter | Crop farmers (n=87) | Office workers (n=80) | p-value* |
|------------------------|----------------------|-----------------------|----------|
| FVC (% pred.)          | 92.4 ± 6.7           | 94.3 ± 9.9            | 0.208    |
| FEV_{1} (% pred.)      | 85.8 ± 9.1           | 87.2 ± 8.9            | 0.312    |
| FEV_{1}/FVC%           | 73.6 ± 4.5           | 74.9 ± 5.1            | 0.079    |
| MEF_{25} % (pred.)     | 57.4 ± 7.3           | 60.7 ± 6.9            | 0.003    |
| MEF_{50} % (pred.)     | 57.8 ± 7.5           | 61.9 ± 7.1            | 0.008    |
| MEF_{75} % (pred.)     | 58.6 ± 6.9           | 62.3 ± 7.2            | 0.001    |
| MEF_{50-75} % (pred.)  | 61.7 ± 7.9           | 64.2 ± 8.3            | 0.047    |

CROP FARMERS

| Sprirometric parameter | Exposed >20 years (n=66) | Exposed ≤20 years (n=21) | p-value* |
|------------------------|---------------------------|--------------------------|----------|
| FVC (% pred.)          | 91.2 ± 9.3                | 92.7 ± 8.4               | 0.516    |
| FEV_{1} (% pred.)      | 84.7 ± 8.5                | 86.1 ± 7.9               | 0.505    |
| FEV_{1}/FVC%           | 72.7 ± 3.3                | 74.4 ± 4.4               | 0.044    |
| MEF_{25} % (pred.)     | 56.9 ± 7.1                | 57.8 ± 6.9               | 0.011    |
| MEF_{50} % (pred.)     | 55.4 ± 6.9                | 58.9 ± 7.1               | 0.047    |
| MEF_{75} % (pred.)     | 56.2 ± 7.3                | 52.3 ± 6.3               | 0.030    |
| MEF_{50-75} % (pred.)  | 59.2 ± 7.2                | 62.8 ± 6.9               | 0.047    |

Mean values of spirometric parameters in crop farmers with exposure duration of more than 20 years, and those with <20 years are given in Table 3.

Results are presented in Table 3 confirm that mean values of spirometric parameters among crop farmers exposed more than 20 years are lower than in those with exposure <20 years with a significant difference for MEF_{50}, and MEF_{75}.

The effect of occupational exposure on crop farmers is monitored by their exposure to certain respiratory hazards, as well as the work activities they perform, at the same time. Data on exposure to respiratory hazards and their occupational activities, such as digging and watering, planting and weeding, harvesting and cleaning of premises, taking into account differences caused by age, gender, and smoking habits.

Table 3 shows the association of several specific work activities in crop farmers with the occurrence of chronic respiratory symptoms.

Logistic regression shows that most of the chronic respiratory symptoms are significantly associated with the most common work activities of crop farmers, such as digging and watering, planting and weeding, harvesting and cleaning of premises, taking into account differences caused by age, gender, and smoking habits.

The distribution of chronic respiratory symptoms associated with workflow characteristics in crop farmers is shown in Table 5, through the prevalence ORs, after adjusting for age, gender, and smoking habits.

Table 5 shows that in the case of all-day exposure among crop farmers, the risk of developing phlegm, dyspnea, and wheezing significantly increases.

The effect of occupational exposure duration to respiratory hazards, smoking, and age on functional lung parameters in crop farmers is shown in Table 6.

Linear regression shows that age, exposure duration, and the combined effect of age, exposure duration, and smoking habit have a significant effect on FEV_{1}, and FEV_{1}/FVC, and have no significant effect on growing cereals and/or industrial crops. Their daily work includes activities such as digging, planting and weeding, watering, harvesting, harvesting of fruits, using agricultural machinery, cleaning workplaces, and so on. In addition, they are exposed to a wide range of respiratory hazards such as dust, temperature amplitudes, pesticides, fertilizers, fodder, exhaust, moisture, draft, and others.

The distribution of chronic respiratory symptoms associated with occupational exposure is shown in Table 5, through the prevalence ORs, after adjusting for age, gender, and smoking habits.

Logistic regression shows that most of the chronic respiratory symptoms are significantly associated with the most common work activities of crop farmers, such as digging and watering, planting and weeding, harvesting and cleaning of premises, taking into account differences caused by age, gender, and smoking habits.

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Table 5: The effect of occupational exposure duration to respiratory hazards on chronic respiratory symptoms.

| Occupation | Chronic respiratory symptoms | OR (95% CI) |
|------------|------------------------------|-------------|
| Digging    | Phlegm                       | 1.29 (0.62–2.63) |
| Watering   | Dyspnea                      | 1.42 (0.67–2.96) |
| Planting   | Wheezing                     | 1.68 (0.81–3.44) |
| Weeding    | Cough                        | 1.78 (0.89–3.63) |
| Harvesting | Symptoms                     | 1.89 (0.90–3.98) |

Table 6: The effect of occupational exposure duration to respiratory hazards on functional lung parameters in crop farmers.

| Occupation | FEV_{1} | FEV_{1}/FVC% | FVC | MEF_{50} | MEF_{75} | MEF_{25} |
|------------|---------|--------------|-----|----------|----------|----------|
| Digging    | 91.2±9.3| 72.7±3.3     | 84.7±8.5| 55.4±6.9 | 56.2±7.3 | 59.2±7.2 |
| Watering   | 92.7±8.4| 74.4±4.4     | 86.1±7.9| 58.9±7.1 | 52.3±6.3 | 62.8±6.9 |

Table 4: Relationship between respiratory symptoms with certain specific work activities of crop farmers, adjusted for age, gender, and smoking habit.

| Symptoms | Digging and watering OR (95% CI) | Planting and weeding OR (95% CI) | Mechanization use OR (95% CI) | Pesticide use OR (95% CI) | Harvesting OR (95% CI) | Cleaning workplaces OR (95% CI) |
|----------|----------------------------------|----------------------------------|-------------------------------|--------------------------|------------------------|-----------------------------|
| Any symptom (1.21–5.16) | 2.50 (1.24–4.68) | 0.81 (0.39–1.75) | 1.38 (0.90–2.14) | 1.92 (1.06–3.49) | 1.39 (1.01–1.92) | 2.35 (1.58–3.50) |
| Cough 2.41 (1.13–4.87) | 2.24 (1.07–4.60) | 1.18 (0.65–2.14) | 1.89 (1.06–3.43) | 1.89 (1.06–3.43) | 1.89 (1.06–3.43) | 2.35 (1.58–3.50) |
| Phlegm 2.26 (1.14–3.39) | 2.05 (1.00–4.03) | 1.65 (0.87–3.14) | 1.78 (1.00–3.14) | 1.78 (1.00–3.14) | 1.78 (1.00–3.14) | 2.09 (1.15–3.77) |
| Dyspnea 2.15 (0.69–4.97) | 1.79 (0.61–4.67) | 1.54 (0.67–3.58) | 1.69 (0.67–4.67) | 1.69 (0.67–4.67) | 1.69 (0.67–4.67) | 2.09 (1.15–3.77) |

Table 4: Relationship between respiratory symptoms with certain specific work activities of crop farmers, adjusted for age, gender, and smoking habit.
Table 5: Distribution of chronic respiratory symptoms related to workflow characteristics in crop farmers (Prevalence ORs [95% CI] *)

| Workflow characteristics | Cough | Phlegm | Dyspnea | Wheezing | Chest tightness |
|--------------------------|-------|--------|---------|----------|----------------|
| All day versus half-day exposure | 1.47 | 1.47 | 1.47 | 1.47 | 1.47 |
| (0.73–3.57) | (0.83–9.45) | (2.32–10.54) | (2.23–21.32) | (0.26–2.84) |
| Exposure to dust | 3.23 | 3.23 | 3.23 | 3.23 | 3.23 |
| (0.75–5.64) | (0.32–2.89) | (0.46–4.47) | (0.57–3.84) | (0.53–3.61) |
| Exhaust gases | 1.14 | 1.14 | 1.14 | 1.14 | 1.14 |
| (0.31–1.37) | (0.41–3.8) | (0.45–3.8) | (0.24–3.59) | (0.46–4.15) |
| Pesticides | 2.23 | 2.23 | 2.23 | 2.23 | 2.23 |
| (1.21–3.73) | (0.28–2.49) | (0.41–2.87) | (0.31–2.32) | 0.05 |
| Cultivated crops | 2.23 | 2.23 | 2.23 | 2.23 | 2.23 |
| Cereal | 2.23 | 2.23 | 2.23 | 2.23 | 2.23 |
| (0.39–2.78) | (0.35–3.7) | (0.73–4.57) | (0.34–2.12) | 0.05 |
| Cereal and industrial | 2.23 | 2.23 | 2.23 | 2.23 | 2.23 |
| (0.19–3.73) | (0.39–2.78) | (0.43–3.39) | (1.11–6.32) | (0.24–4.98) |

Data are given as odds ratios with 95% confidence intervals. *p<0.05; OR: Odds ratio; CI: Confidence interval. *Tested by logistic regression after adjustment for age, gender, and smoking habit.

Discussion

Our study evaluated the effects of specific work activities and occupational exposure to respiratory hazards on the occurrence of chronic respiratory symptoms and lung functional impairments among exposed crop farmers. The CG consists of an adequate number of unexposed persons (office workers) complementary to those exposed by sex and age. In both groups, there is a relatively high prevalence of active smokers (about 50%) and is slightly higher than in the previous studies by Stoleski et al. among agricultural workers [27], [28], [29].

The prevalence of subjects with chronic respiratory symptoms in our study, among EG was 43.7%, of which approximately 68% indicated their work-related exacerbation. The prevalence of subjects in CG with respiratory symptoms was 28.7%, with no association of symptoms with work. The prevalence of overall symptoms was higher in EG subjects, and a significant difference was reported for cough, phlegm, and dyspnea. In a study of 240 feed production workers exposed to high average dust concentration (16.8 mg/m3), Kuchuk et al. report a prevalence of chronic bronchitis of 26.4% [19].

Chronic respiratory and nasal symptoms and chronic pulmonary diseases still represent important clinical and public health problems for agricultural workers [1]. According to studies across Europe, the prevalence of chronic respiratory symptoms varies from 25% to 35% [30], while according to research by Stoleski et al. dedicated to agricultural workers in the Skopje region, it is 26.6% [27]. The prevalence of phlegm in farmers in the above-mentioned study was 8.3%, which is similar not only to some previous studies in our country dedicated to the respiratory effects caused by specific occupational exposure in agricultural workers but also to those in Slovenia and Croatia [31]. According to the results of a Dutch study, the incidence of phlegm in farmers is 2–12% depending on the main activity; it is highest among livestock breeders [30]. The prevalence of phlegm in Finnish farmers is 7.5% [32], up to 23%, according to a study in Manitoba, Canada [33]. According to the results of a Finnish study conducted as a follow-up after 3 years, the prevalence of phlegm is higher, with an annual incidence rate of 2%. The survey in Denmark included a sample of 834 men from the general population, aged 65–84 years, with the highest prevalence of phlegm among retired agricultural workers [34].

Research in France shows the highest prevalence of dyspnea among farmers (37%), industrial workers (31%), and lowest among teachers (15%) [35], similar to studies showing a higher frequency of chronic cough among farmers [36], [37]. A survey in Poland examining cereal growers (sowing, irrigation, harvesting, and collecting) showed a prevalence of 44.7% for chronic respiratory symptoms, with the highest rates being recorded for chronic cough (26.3%) and dyspnea (19.7%) [38]. Many other studies also confirm the high prevalence of wheezing among agricultural workers compared to office workers [39]. In the study of Stoleski et al. [27], a higher prevalence of overall chronic respiratory symptoms in agriculture compared to office

Table 6: Effect of exposure duration, smoking habit, and age on spirometric parameters in crop farmers

| Spirometric parameters | FVC | PEFR | MEF₂₅ | MEF₅₀ | MEF₇₅ |
|------------------------|-----|------|-------|-------|-------|
| Age | 0.0172247 | 10.3887824 | 0.04 | 0.70 |
| Exposure duration | 0.0001123 | 7.30622185 | 0.00 | 0.57 |
| Smoking habit (cigarettes/daily/years smoking) | 0.00168625 | 6.16975000 | 0.11 | 0.49 |
| Combined effect of age, exposure duration, and smoking habit | 0.02204462 | 12.046138454 | 0.12 | 0.76 |
| FEV₁ | 0.2437322 | 9.453903620 | 0.50 | 0.00 |
| Exposure duration | 0.6117875 | 6.079863027 | 0.34 | 0.02 |
| Smoking habit (cigarettes/daily/years smoking) | 0.00244532 | 4.50717500 | 0.12 | 0.42 |
| Combined effect of age, exposure duration, and smoking habit | 0.26430133 | 9.50527486 | 0.64 | 0.00 |
| FEV₁/FVC | 0.5176680 | 8.655308450 | 0.72 | 0.00 |
| Exposure duration | 0.00115650 | 7.70675000 | 0.16 | 0.45 |
| Smoking habit (cigarettes/daily/years smoking) | 0.5382050 | 6.503906583 | 0.53 | 0.00 |
| Combined effect of age, exposure duration, and smoking habit | 0.17156695 | 9.349037257 | 0.49 | 0.09 |
| MEF₅₀ | 8.424421459 | 0.1053786 | 0.32 | 0.00 |
| Exposure duration | 0.00590565 | 5.435906790 | 0.19 | 0.07 |
| Smoking habit (cigarettes/daily/years smoking) | 0.01254350 | 4.55125000 | 0.08 | 0.59 |
| Combined effect of age, exposure duration, and smoking habit | 0.01254350 | 4.55125000 | 0.12 | 0.59 |

FVC: Forced vital capacity; PEFR: Forced expiratory flow in one second; MEF₂₅, MEF₅₀, MEF₇₅: Maximal expiratory flow at 25–75%, 50%, and 75% of FVC, respectively. *p<0.05; **Tested by multiple linear regression.
workers has been found, with a significant difference for cough and wheezing.

According to the study by Stoleski et al. about chronic respiratory symptoms and bronchial hyperreactivity in agricultural workers in the R. Macedonia, with particular reference to their intensity and relationship to occupational exposure [28], the prevalence of overall chronic respiratory symptoms in cattle breeders is 31.6%, which is similar to surveys across Europe, where their frequency varies with farmers from 25% to 35% [30]. In general, many studies around the world, such as those conducted in New Zealand, Germany, Spain, and other countries [36], [40], [41], confirm the higher prevalence of work-related chronic respiratory symptoms in farmers, and certain differences are likely due to regional differences, differences in exposure or possibly the use of different farming and livestock methods and techniques of operation. Studies in this regard show a higher prevalence of chronic bronchitis in livestock and cattle breeders compared to farmworkers [19]. The prevalence of overall respiratory symptoms in the study by Stoleski et al. dedicated to the impact of smoking and the length of occupational exposure on respiratory symptoms and lung functional impairments among farmworkers [29] accounted for 29.3%. Cough is present at 20%, phlegm in 10.7%, while the prevalence of dyspnea, wheezing, and chest tightness is 12%, 10.7%, and 8%, which is quite similar to the prevalence of registered self-reported respiratory symptoms in a study of European animal farmers [42], confirming the association between occupational exposure and the development of chronic respiratory symptoms.

In this regard, the study by Danuser et al. concludes that agricultural work in Swiss farmers is closely linked to the risk of developing chronic bronchitis and four and a half times higher risk of phlegm compared to the general population [43]. In any case, the prevalence of chronic respiratory symptoms does not always correspond to the degree of impaired airflow detected by spirometry.

Another study examining, the prevalence of chronic bronchitis among agricultural workers is that of Kern et al. [44]. It includes subjects working on a farm but not involved in livestock breeding, and the results are compared with those engaged in food packaging. The study found a significantly higher prevalence of chronic bronchitis in men in the study group (20.9%) compared with the CG (7.4%). On the other hand, smokers had a significantly higher prevalence of chronic bronchitis (30.2%) compared to non-smokers (6.9%).

Significantly, the higher incidence of respiratory symptoms in men than in women exists only in EG. The prevalence of phlegm in both groups was significantly higher in men. The results are similar to those in studies with respondents with specific occupational exposure to organic and inorganic dust [45].

The risk of developing respiratory symptoms is approximately 3 times higher in EG subjects with exposure more than 20 years, compared to those with shorter exposure. The risk of developing respiratory symptoms is about 3 times higher in exposed subjects in EG who are active smokers compared to nonsmokers. Out of the individual chronic respiratory symptoms, the length of exposure over 20 years in EG is significantly associated with cough and phlegm, whereas active smoking correlates significantly with cough and phlegm. A significant association between exposure length and chronic bronchitis has been reported in the study by Omland et al. with 1691 farmers exposed to vegetable and animal dust [46]. Chronic respiratory symptoms in agricultural workers in the study of Stoleski et al. [27] are significantly related to the length of occupational exposure over 20 years, age over 60 years, exposure to chemical hazards, and smoking habits in men. Many studies indicate a higher frequency of chronic respiratory symptoms in agricultural workers with long-term occupational exposure [47], while those examining the respiratory effects of different types of organic dust speak of a significant association between smoking habit and chronic respiratory symptoms [48], [49].

Farmers' research in France shows a synergistic effect of occupational exposure and smoking, especially for cough and phlegm, while a similar study in Canada indicates a significant association between phlegm, dyspnea, and wheezing among agricultural workers [33]. In the study of Stoleski et al., the incidence of active smokers among agricultural workers is 26.7%, and the frequency of respiratory symptoms in the past 12 months is higher among agricultural workers with exposure longer than 15 years, but with statistical significance only for overall respiratory symptoms and dyspnea [29].

In the study of Kuchuk et al. among workers engaged in animal feed production, there was a significantly higher prevalence of airflow obstruction in exposed than in non-exposed subjects, being significantly associated with respirable workplace dust concentration [19].

The results of our study indicate lower mean values of all spirometric parameters, with a significant difference for mean values of the small airways parameters (MEF_{25}, MEF_{50}, MEF_{75}, and MEF_{25-75}) in EG compared to CG subjects. The mean values of spirometric parameters were lower in EG subjects exposed longer than 20 years compared to those with shorter exposure, with statistical significance for FEV_{1}/FVC%, MEF_{25}%, MEF_{50}%, and MEF_{75}%. There is a significant difference in the detected ventilatory insufficiency in EG compared to CG for obstructive, combined, predominantly obstructive type of ventilator insufficiency, as well as small airways obstruction. The results are similar to several studies conducted in our country and worldwide with subjects from the general population and subjects with specific occupational exposure [50]. According to the study
by Karadzinska-Bislimovska et al. among agricultural workers, the prevalence of lung functional impairment is from 23.4% to 28.8% [14], while Stoleski et al. in a survey of agricultural workers in rural areas show that respiratory diseases are among the most common, with a prevalence of 23.8% [15].

A Canadian study of agricultural workers, mainly engaged in cereal cultivation in Manitoba, shows a non-significant difference in basic spirometric parameters (VC, FEV1, and Tiffeneau index) compared to controls, although they are much lower in agricultural workers [33]. The research of Stoleski et al. in agricultural workers in the Skopje region shows lower mean values of all spirometric parameters than the CG, with a significant difference for the mean values of MEF25 and MEF75, and ventilatory disorders are associated with age over 60, length of occupational exposure over 20 years, smoking habit, and exposure to dust and pesticides [27]. On the other hand, the research of Dosman et al. [51] on the effect of specific occupational exposure on the frequency of chronic respiratory symptoms and the reduction of functional lung parameters in workers engaged in cereal cultivation in Denmark, recorded significantly lower values of all spirometric parameters (including small airways) compared to controls, and their decrease is significantly related to age and exposure to pesticides. Similar results were obtained in the study of Corey et al., Enarson et al., and Huy et al., regarding the effect of grain dust on the values of spirometric parameters in exposed agricultural workers [52], [53], [54]. Significantly lower VC and FEV1 values in livestock breeders compared to controls were reported in the study by Dalphin et al., exploring the effects of specific occupational exposure in France [55]. Research on agricultural workers in Serbia shows an annual decrease in the value of FEV1 to 44 ml [56]. According to a longitudinal Canadian study of farmworkers in barns and silos, the first decline in the value of FEV1 was recorded after a 2.5–3-year exposure, followed by a progressive further decline in ventilation [39]. The longitudinal study of Dalphin et al. among farmers in France reveals a significant correlation between the decrease in Tiffeneau index values (FEV1/FVC%) with the intensity and length of occupational exposure to organic dust [57]. The mentioned study of farmers in Serbia recorded significantly reduced FVC and FEV1 values compared to control workers, without identifying the effect of smoking habit [56]. The synergy between specific occupational exposure and smoking has been confirmed in many other studies dealing with the respiratory health of agricultural workers. According to the longitudinal study of Tashkin et al. [58], the annual decrease in the value of FEV1 is between 7 and 33 mL, depending on the length and intensity of occupational exposure to aeropollutants and tobacco smoke.

In the actual study, obstructive patterns in the small airways in EG were significantly related to the length of exposure, active smoking, and length of smoking experience. The association between obstructive ventilatory insufficiency and small airways obstructive patterns with active smoking among CG subjects is non-significant, suggesting a possible interaction between occupational exposure and tobacco smoke in their occurrence in EG subjects.

The combined effect of smoking, it’s duration, and the number of cigarettes smoked per day significantly influence the occurrence of obstructive pattern in the small airways of the EG subjects, while small airways obstructive pattern is significantly associated with the occurrence of cough and phlegm in EG1 and with chronic bronchitis in CG. Similar findings are reported in the study by Omland et al. which investigates the respiratory effects of occupational exposure on farmers [46]. The study by Kuchuk et al. with animal feed production workers exposed to high concentrations of respiratory dust suggests a significant association between obstructive ventilatory insufficiency and small airways obstruction with exposure duration and smoking [19]. The research of Stoleski et al. about chronic respiratory symptoms and bronchial hyperresponsiveness in agricultural workers in the R. Macedonia, with particular reference to their intensity and relationship with occupational exposure, registered lower mean values of spirometric parameters in cattle breeders compared to farmers, with statistical significance for the mean values of MEF25 and MEF75. According to this study, ventilatory disorders are associated with over age 55, smoking habit and occupational exposure to dust, gases, vapors, and pesticides over 25 years [28].

Sigsgaard et al. in the Danish study, young farmers, reported a significant difference between men farmers and men in the CG, while in women farmers basic spirometric parameters were significantly lower than women in the CG [59]. Our previous research [29] confirms the decline in lung functional parameters with increasing the length of exposure, but statistical significance exists only for MEF25 and MEF75. According to this study, ventilatory disorders are associated with over age 55, smoking habit and occupational exposure to dust, gases, vapors, and pesticides over 25 years [28].

Gautrin et al. in Canada suggest that there is a positive interaction effect between occupational exposure to cereal cultivation and smoking habit on lung function and the prevalence of chronic bronchitis in women [60]. The research of Stoleski et al. [29] shows a significant association between small airway flow and the combined effect of exposure length, smoking, smoking experience, and number of cigarettes smoked in exposed workers. Furthermore, the research shows that exposure length, smoking, and age have an independent effect only on small airway flow, i.e., on MEF25,75 indices, and not on other spirometric parameters (FVC, FEV1, and FEV1/FVC%) [29].

The prevalence of chronic bronchitis and COPD development has also been studied by Eduard et al. who compared cereal farmers and livestock breeders [61]. They conclude that ranchers suffer from both conditions
and have a risk of 1.9 for chronic bronchitis and 1.4 for COPD. Earlier research shows that farm dust exposure is associated with COPD development [62]. Analyzing chronic bronchitis in Swiss farmers, Danuser et al. [43] reported a prevalence rate of 16% and showed a significant increase with age. The most important risk factors for the development of chronic bronchitis are cereal cultivation, age over 60 years, smoking, and indoor exposure longer than 4 h a day. The prevalence of chronic bronchitis among non-smoker farmers in Switzerland is 12% and is significantly higher than in the general population (6.8%).

The effect of occupational exposure in crop farmers in our study is evaluated through their exposure to certain respiratory hazards and by their work activities, exposure to each hazard individually, and combined exposure to several occupational respiratory hazards at the same time. Data are obtained by the self-reported questionnaire on occupational exposure to respiratory hazards. Logistic regression analysis shows that most of the chronic respiratory symptoms are significantly associated with the most common work activities.

Furthermore, certain work processes, such as exposure to dust, smoke, gases, pesticides, and day-to-day activity in crop farmers, and exposure to disinfectants, dust, gases, and vapors, significantly increase the risk of certain chronic respiratory symptoms. Significant effects on age, length of exposure and the combined effect of age, and length of exposure and smoking on individual spirometric parameters were also recorded in EG subjects, and positive, and inverse correlations between mean spirometric parameters were also found, in terms of demographics, smoking habits, and exposure to respiratory hazards among crop farmers.

The Italian study by Talini et al. [37] reported a significant role for certain specific work activities in increasing the prevalence of certain respiratory symptoms, mainly cough and phlegm. These work activities are strongly associated with exposure to endotoxins and organic dust, thus suggesting the possible role of these agents in the etiology of chronic bronchitis. Our previous research indicates a significant association between most chronic respiratory symptoms and plant growing and irrigation [27]. All-day exposure to respiratory hazards in crop farmers is a significant predictive factor for the development of phlegm, dyspnea, and wheezing. In the study of Stoleski et al. [28], subjects who had contact with animals during working hours were up to 5 times more likely to have asthma symptoms than crop farmers, while respiratory symptoms typical of chronic bronchitis are 3 times more common. An Iranian study [63], after adjusting for certain confounding variables, shows that pesticide use in farmers is significantly related to the development of work-related chronic respiratory symptoms. According to the study by Koceva [64], most of the examined parameters in farmers are statistically significantly related to age over 60 years, exposure duration more than 25 years, smoking, smoking experience of more than 20 years, and exposure to chemical hazards (dust, vegetable particles, animal fibers, and pesticides).

Technological advances in agriculture have greatly improved working conditions, but paradoxically increased the intensity and frequency of exposure, such as exposure to organic dust [65], [66]. In addition, engineering controls are often insufficient, the use of safeguards is often inadequate, and occupational exposure to traditional hazards is still dominant as agricultural activities and procedures are not fully standardized, although most of the working population participates in a certain type of agricultural activity [40], [67].

A relatively small number of subjects in the study groups and lack of ambient monitoring may be certain study limitations, with the possibility to interfere with results and potentially aggravate a clear relationship between occupational exposure and respiratory impairment in crop farmers.

Conclusion

The study results revealed a higher prevalence of respiratory symptoms, and significantly lower values of small airways indices in crop farmers compared to controls and their relation to exposure duration. The results recognized the role of occupational exposure in the development of respiratory symptoms and lung function decline, and confirmed that exposure together with specific workflow activities may be predictors of respiratory health impairment among crop farmers. On the other hand, information on respiratory health in crop farmers is not readily available, and statistics do not always provide a complete picture of the prevalence of chronic respiratory symptoms and diseases due to inadequate reporting or inaccessibility of relevant data. It is therefore necessary to establish their association with specific occupational exposure in agriculture, to apply protocols for their evaluation and to emphasize prevention strategies. These actions should further contribute in critical points detection and indicate the need for adequate preventive measures with obligatory use of respiratory protective equipment, and implementation of engineering controls.

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