

## PREVALENCE AND CHARACTERISTICS OF CHRONIC RESPIRATORY SYMPTOMS AND LUNG FUNCTION AMONG VINEYARD WORKERS

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### Abstract

**Introduction:** Working activities in viticulture are accompanied by exposure to numerous occupational respiratory hazards that can cause damage to the respiratory system, but also to other organs and systems.

**Aim of the study:** To determine the frequency of chronic respiratory symptoms and ventilatory function in a group of vineyard workers.

**Material and methods:** The study included 45 vineyard workers. All of them completed the questionnaire on the occurrence of respiratory symptoms and underwent spirometric testing, while occupational exposure was evaluated with job exposure matrices for respiratory hazards.

**Results:** A high frequency of active smokers (57%) and a relatively low frequency of ex-smokers (15%) were registered. Preventive health examinations of different types were performed in most subjects (over 80%) at different time intervals. Most of the vineyard workers believe that they are sufficiently informed about the health risks related to their work activities and the necessary measures needed for health protection. Also, most of them use the mandatory personal protective equipment, while almost all workers during their work, to a greater or lesser extent, were exposed to occupational respiratory hazards: dust, smoke, fumes, gases and pesticides. About 45% of subjects had one or more respiratory symptoms, and the most common symptoms were cough (40%), cough with phlegm (31.1%), as well as dyspnea and wheezing (22.2%). The frequency of chronic respiratory symptoms was higher in workers with more than 15 years of exposure, with a statistically significant difference in frequency of cough, cough with phlegm, and dyspnea. The risk of respiratory symptoms was about 3 times higher in active smokers and about 2 times higher in vineyard workers with exposure duration longer than 15 years. The mean values of all spirometric parameters were within the reference values, while lung function impairment of obstructive, restrictive and combined pattern was registered in about 20% of them. The mean values of spirometric parameters in vineyard workers with exposure duration longer than 15 years were lower than those with less than 15 years of experience, with a significant difference for small airways flow indices. Most subjects were regularly exposed to moderate levels of dust and rarely and occasionally exposed to low to medium levels of gases/fumes/vapors and pesticides.

**Conclusion:** Higher frequency of respiratory symptoms and lung function abnormalities were registered in the vineyard workers. The obtained results indicate the need to improve preventive measures in order to reduce the work-related health risks.

**Keywords:** ventilatory function, viticulturists, smoking, respiratory symptoms, spirometry, job exposure matrices

## Introduction

Viticulture refers to the cultivation of grapes, either for consumption or for making wine, and deals with the study and production of grapes, encompassing everything that take place in the vineyard. The vineyard worker's calendar includes the study of the grapes that are harvested and transported to the winery, pruning the vines in winter, plowing the soil to loosen it and expose the base of the vines, their flowering, and pruning the vines to obtain grapes in summer. Vineyard workers do not produce wines, but only supervise and study the growth process<sup>[1]</sup>. In Macedonia, grapevine began to be cultivated under the dominance of Mediterranean civilizations, and the greatest influence was exerted by the Roman Empire. The success of viticulture and winemaking is primarily conditioned by the existence of favorable agro-ecological conditions, which in the Republic of Macedonia are present and enable uninterrupted and high-quality cultivation of a large number of varieties, both table and wine grape<sup>[2]</sup>.

Vineyard workers have potential exposures to a very wide range of agents that are inhaled: inorganic dust from the soil; organic dust containing microorganisms, mycotoxins or allergens; decomposition gases; pesticides, etc. The variety of exposures and the circumstances in which they occur can result in different degrees and types of respiratory response<sup>[3]</sup>. Modern agriculture involves many different types of exposures to the respiratory system. While most exposures, such as those to dust, bacteria, endotoxins, and spores, occur primarily in the workplace, other hazards, such as storage mites, can be encountered not only in the workplace but also in the home environment, and exposure to various chemicals can occur in fields, yards, gardens, or at home<sup>[4]</sup>. The impact on the respiratory system can also vary considerably. Exposure to airborne substances can affect the airways and, depending on the antigenic potential of the substances and the susceptibility of the host, can result in asthma, an asthma-like syndrome, or chronic obstructive pulmonary disease<sup>[5]</sup>. According to current knowledge, a distinction has been made between asthma and asthma-like syndrome, based on the view that asthma is a relatively progressive condition often associated with antigenic exposure. On the other hand, asthma-like syndrome suggests mild, mostly reversible airway obstruction in the context of a transient or mild increase in nonspecific bronchial reactivity that primarily results from nonantigenic exposures<sup>[6]</sup>.

Respiratory health and lung function are critical components of overall well-being, particularly for individuals whose work environments expose them to unique occupational hazards<sup>[7]</sup>. Vineyard workers often face prolonged exposure to dust, pesticides, and other airborne particles that can significantly impact respiratory health. Despite the growing attention to occupational safety in agriculture, the respiratory challenges faced by vineyard workers remain an underexplored area of study. Understanding the risks, identifying preventive measures, and promoting awareness of respiratory health in this sector are crucial for safeguarding the workforce and ensuring sustainable agricultural practices<sup>[8]</sup>.

Occupational exposure to respiratory hazards in agricultural settings has been well documented, with evidence linking such exposures to a range of chronic respiratory conditions<sup>[9]</sup>. Vineyard workers, in particular, are subjected to multiple inhalational agents, including organic and inorganic dusts, pesticides, fungal spores, and pollens, as well as variable climatic conditions

that may exacerbate airway inflammation and compromise pulmonary function over time. Despite these recognized risks, there remains a paucity of data specifically addressing respiratory health outcomes in this subset of agricultural workers<sup>[4]</sup>.

Previous studies in similar occupational groups have demonstrated elevated prevalence rates of chronic bronchitis, wheezing, dyspnea, and other lower respiratory tract symptoms, often associated with measurable declines in lung function parameters such as forced vital capacity (FVC) and forced expiratory volume in one second (FEV<sub>1</sub>)<sup>[5,10]</sup>. However, vineyard work presents unique exposure profiles related to viticulture practices; yet this population has not been sufficiently characterized in terms of chronic respiratory morbidity and lung function impairment<sup>[11,12]</sup>.

The study objective was to determine the frequency of chronic respiratory symptoms and lung function in a group of vineyard workers, to determine the relationship between chronic respiratory symptoms and the values of pulmonary functional parameters with certain characteristics of the studied workers (age, duration of exposure, smoking, length of smoking experience and specific occupational exposure), to determine the characteristics of occupational exposure by applying occupational exposure matrices, as well as to define recommendations for the prevention of chronic respiratory disorders and the promotion of respiratory health among vineyard workers. By identifying the respiratory health burden in this population, the findings may contribute to improved occupational health surveillance, early intervention strategies, and the development of evidence-based preventive measures tailored to viticulture.

## **Subjects and Methods**

### ***Study design and setting***

A cross-sectional study was conducted in the Center for Respiratory Functional Diagnostics by the team from the Institute for Occupational Health, Skopje in the period from March 2019 to February 2020, when the data collection was terminated due to Covid-19 pandemic outbreak.

### ***Study population***

This cross-sectional study included 45 vineyard workers (mean age =  $48.1 \pm 11.8$  years, range: 24-65 years) from the Tikvesh region, who were registered and worked as individual farmers or were associated in cooperatives (mean exposure duration  $23.4 \pm 10.2$  years, range: 1-38 years). Within the framework of their job activities, they were engaged to work mainly in open space for cultivating and growing vines, i.e. for growing grapes, both for eating and wine production. Their daily work included activities such as: digging, planting and weeding, watering, harvesting grapes and transporting them to the wineries, pruning the vineyards in winter, plowing the soil to loosen it and uncover the base of the vineyards, their flowering and pruning the vineyards to obtain grapes in summer, cleaning work areas, etc.

The effect of occupational exposure among the examined vineyard workers was monitored through their exposure to a specific respiratory hazard and according to their work activities, that is, exposure to each hazard individually, but also combinations of exposure to several occupational respiratory hazards simultaneously. The study used data on exposure to respiratory hazards as well as the work activities they performed, along with a detailed work history.

In doing so, they were exposed to a wide range of respiratory hazards such as: dust, temperature changes, pesticides, artificial fertilizers, exhaust gases, moisture, drafts and others. Exposure to occupational respiratory hazards (dust, gases, fumes, vapors, pesticides) for each

respondent was estimated according to data from the matrix for occupational exposure to respiratory hazards, making it consistent with certain work activities among agricultural workers. Inclusion criteria: persons aged 18 to 65 years, male or female, engaged in viticulture, who were exposed to at least one occupational respiratory hazard (dust, gases, fumes, vapors, pesticides) during their work.

Exclusion criteria: persons younger than 18 or older than 65 years, persons not engaged in viticulture. In order to avoid selection bias and errors in the results of the study, persons aged 18-65 years who were exposed to respiratory hazards related to other work activities, not only viticulture, were not included.

Depending on the duration of exposure, the examined workers were divided into two subgroups: those exposed for less than 15 years and those exposed for more than 15 years. The study did not comprise any person in whom spirometry testing was contraindicated. The Institute's Ethics Committee approved the content of our study protocol, whereas all examined subjects were informed about the objectives of the study and were willing to participate in the study.

#### ***Study protocol - Questionnaire***

All study subjects were interviewed by a physician and completed a standardized questionnaire including questions on work history, respiratory symptoms in the last 12 months, and smoking habit. Chronic respiratory symptoms in the last 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 (ECRHS) questionnaire<sup>[1314]</sup>. Classification of smoking status was done according to the World Health Organization (WHO) guidelines on definitions of smoking status<sup>[15]</sup>. 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 the daily mean of cigarettes smoked were also assessed. Pack-years smoked were calculated according to the actual recommendations<sup>[16]</sup>. An ex-smoker was defined as a former daily smoker, who no longer smokes. Passive smoking or exposure to environmental tobacco smoke (ETS) was defined as the exposure of a person to tobacco combustion products from smoking by others<sup>[17]</sup>.

#### ***Baseline spirometry***

All study subjects underwent spirometry testing, performed with the spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany), measuring forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC ratio, and maximal expiratory flow at 50%, 75%, and 25-75% of FVC (MEF50, MEF75, and MEF25-75, respectively), by recording the best result of three measurements of FEV1 values within 5% of each other. The results were expressed as percentages of the predicted values according to the European Community for Coal and Steel (ECCS) norms. The spirometry results were given as percent of their predicted values due to the current European Respiratory Society (ERS) and American Thoracic Society (ATS) recommendations, including reproducibility and acceptability<sup>[18]</sup>.

#### ***Job exposure matrices***

To assess occupational exposure to respiratory agents among dairy farmers, we used job exposure matrices recommended by the European Association of Schools of Occupational Medicine (EASOM), both qualitative matrix, and quantitative matrix with exposure intensity and exposure frequency<sup>[19]</sup>.

### Statistical analysis

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. A P-value of less than 0.05 was considered statistically significant. Logistic regression analysis was used to assess the risk for chronic respiratory symptoms, asthma and COPD development within job-exposure matrices, adjusted for age and smoking habit. Study variables were checked for normality by Kolmogorov-Smirnov and Shapiro-Wilk's W test.

### Results

The study population included 45 vineyard workers, 31(68.9%) men and 14(31.1%) women, aged 24-65 years. The data obtained from the work history of the surveyed vineyard workers were of particular importance for the current study. Their average total work experience was  $25.3 \pm 12.8$  years, and the average experience at the current job position was  $23.4 \pm 10.2$  years. All subjects were exposed to occupational respiratory hazards to a greater or lesser extent during their work: dust, fumes, vapors, gases and pesticides.

The examined subjects were recruited during their preventive check-ups at the Institute for Occupational Health of R. North Macedonia - Skopje.

The demographic characteristics of the subjects are shown in Table 1.

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

Variables	Subjects (n=45)
Gender	Males 31 (68.9%) Females 14 (31.1%)
Ratio males/females	2.2
Age (years)	$48.1 \pm 11.8$ range (24-65)
Total work experience (years)	$25.3 \pm 12.8$ range (1-42)
Work experience at current job position (years)	$23.4 \pm 10.2$ range (1-38)
Exposure length longer than 15 years	32 (71.1%)
<i>Place of residence</i>	
City	6 (13.3%)
Village	39 (86.7%)
<i>Home heating method</i>	
- Wood and/or coal	37 (82.2%)
- Electric current	8 (17.8%)

Frequencies are shown as the number and percentage of subjects with certain variable. Numerical data are expressed as mean value with standard deviation.

Smoking status is shown in Table 2. The survey registered 26(57.7%) active smokers with an average smoking experience of  $21.7 \pm 8.3$  years, and the average number of cigarettes smoked during the day was  $18.3 \pm 10.4$  cigarettes/day. Former smokers (15.5%) had an average smoking

experience of  $10.1 \pm 6.5$  years, with  $17.4 \pm 10.3$  cigarettes smoked/day, as the average number of cigarettes, during the period when they smoked, while a relatively small proportion of subjects (20%) were passively exposed to tobacco smoke.

**Table 2.** Smoking status in vineyard workers

Smoking status	Subjects (n=45)
Active smokers	26(57.7%)
Smoking experience (years)	$21.7 \pm 8.3$
range (years)	(3 - 41)
Average number of cigarettes per day	$18.3 \pm 10.4$
range (years)	(6-40)
Ex-smokers	7(15.5%)
Smoking experience of former smokers (years)	$10.1 \pm 6.5$
range (years)	(2 - 23)
Average number of cigarettes among former smokers	$17.4 \pm 10.3$
range (years)	(4 - 30)
Passive smokers	9(20%)

Frequencies are shown as the number and percentage of subjects with certain variable. Numerical data are expressed as mean value with standard deviation.

The most common respiratory symptoms in vineyard workers were: cough (40%), cough with phlegm (31.1%), as well as dyspnea and wheezing (22.2%). It is important to note that chronic respiratory symptoms in 8 (17.8%) subjects were more pronounced while at work. The frequency of chronic respiratory symptoms is presented in Table 3.

**Table 3.** Frequency of chronic respiratory symptoms in vineyard workers

Respiratory symptoms	Subjects (n=45)
Overall respiratory symptoms in the last 12 months	21 (44.4%)
Wheezing at any time in the last 12 months	10(22.2%)
Wheezing followed by shortness of breath or dyspnea in the last 12 months	8(17.8)
Chest tightness in the last 12 months	7(15.6%)
Shortness of breath or dyspnea in the last 12 months	10(22.2%)
Dry cough in the last 12 months	18(40%)
Cough with phlegm for at least 3 months each year or in the last 12 months	14(31.1%)
Cough with phlegm for at least 3 months in at least two consecutive years	11(24.4%)
Worsened symptoms during work	8(17.8%)

Frequencies are shown as the number and percentage of subjects with certain variable.

**Table 4.** Frequency of chronic respiratory symptoms in the last 12 months in vineyards workers according to the length of exposure

Respiratory symptoms in the last 12 months	Exposed $\geq 16$ years (n = 32)	Exposed $\leq 15$ years (n = 13)	P-value*
Any respiratory symptom	16 (50%)	5 (38.5%)	0.488
Cough	15 (46.8%)	3 (23.1%)	0.048*
Cough with phlegm	10 (31.2%)	1 (7.7%)	0.039*
Dyspnea	9 (28.1%)	1 (7.7%)	0.047*
Wheezing	8 (25%)	2 (15.4%)	0.298
Chest tightness	5 (15.7%)	2 (15.4%)	0.946

Frequencies are shown as the number and percentage of subjects with certain variable.

\* Tested by chi square test or by Fisher's exact test.

The frequency of chronic respiratory symptoms in the last 12 months was higher among vineyard workers with an exposure experience of more than 15 years compared to those with an exposure experience less than 15 years, with a significant difference found for cough, cough with phlegm, and dyspnea (Table 4).

The association of respiratory symptoms with the duration of exposure and with active and passive smoking among the examined vineyard workers is shown in Table 5.

**Table 5.** Association between exposure duration and active and passive smoking with respiratory symptoms in the last 12 months among the examined vineyard workers

Variable	n = 45	P- value *
Exposure duration ≤15 years with respiratory symptoms	5/13 (38.5%)	P=0.488
Exposure duration ≥16 years with respiratory symptoms	16/32 (50%)	
Active smokers with respiratory symptoms	22/26 (84.6%)	P=0.021*
Active smokers without respiratory symptoms	4/26 (15.4%)	
Passive smokers with respiratory symptoms	6/9 (66.7%)	P=0.354
Passive smokers without respiratory symptoms	3/9 (33.3%)	

Frequencies are shown as the number and percentage of subjects with certain variable.

\* Tested by chi square test.

The risk of respiratory symptoms was about 3 times higher in active smokers compared to non-smokers (OR=3.20 (0.95-11.41) CI 95%), and about 2 times higher in vineyard workers with exposure duration longer than 15 years compared to those with shorter duration of exposure (OR=2.16 (0.63-9.89) CI 95%).

Table 6 gives an overview of mean values of spirometric parameters among examined vineyard workers.

**Table 6.** Mean values of spirometric parameters

Spirometric parameter (% of predicted value)	Mean value
FVC (% pred.)	93.1 ± 9.6
FEV <sub>1</sub> (% pred.)	86.2 ± 8.8
FEV <sub>1</sub> /FVC%	73.4 ± 4.9
MEF <sub>25</sub> (% pred.)	57.9 ± 7.1
MEF <sub>50</sub> (% pred.)	58.2 ± 7.2
MEF <sub>75</sub> (% pred.)	59.2 ± 6.7
MEF <sub>25-75</sub> (% pred.)	61.9 ± 7.9

Numerical data are expressed as mean value with standard deviation.

FVC: forced vital capacity; FEV<sub>1</sub>: forced expiratory volume in 1 second; MEF<sub>25</sub>, MEF<sub>50</sub>, MEF<sub>75</sub>, MEF<sub>25-75</sub>: maximum expiratory flow rate at 25%, 50%, 75% and 25-75% of FVC, accordingly; % pred: % of predicted value.

The mean values of spirometric parameters in vineyard workers with exposure duration greater than 15 years were lower compared to those with exposure duration less than 15 years, with a significant difference for airflow in small airways (MEF<sub>50</sub>, MEF<sub>75</sub> and MEF<sub>25-75</sub>) (Table 7).

**Table 7.** Mean values of spirometric parameters in vineyards workers according to length of exposure

Spirometric parameters	Exposed ≥ 15 years (n = 32)	Exposed ≤ 15 years (n = 13)	P-value*
FVC (% pred.)	92.3 ± 9.1	94.2 ± 8.9	0.322

FEV <sub>1</sub> (% pred.)	84.8 ± 8.1	86.7 ± 7.8	0.267
FEV <sub>1</sub> /FVC%	71.3 ± 4.7	73.9 ± 4.2	0.080
MEF <sub>50</sub> (% pred.)	55.9 ± 6.1	60.2 ± 6.8	0.041*
MEF <sub>75</sub> (% pred.)	52.2 ± 5.9	59.6 ± 6.4	0.029*
MEF <sub>25-75</sub> (% pred.)	57.8 ± 7.9	62.3 ± 8.1	0.038*

Numerical data are expressed as mean value with standard deviation. FVC: forced vital capacity; FEV<sub>1</sub>: forced expiratory volume in 1 second; MEF<sub>25</sub>, MEF<sub>50</sub>, MEF<sub>75</sub>, MEF<sub>25-75</sub>: maximum expiratory flow rate at 25%, 50%, 75% and 25-75% of FVC, accordingly; % pred: % of predicted value. \* Tested by t-test for independent samples.

The relationship between the obstructive ventilator pattern, duration of exposure and active smoking among examined vineyard workers is illustrated in Table 8.

**Table 8.** Relationship between obstructive ventilatory pattern, exposure duration and active smoking among vineyard workers

Variable	n = 45	P-value*
Exposure duration ≤15 years with obstructive ventilatory pattern	1/13 (7.7%)	0.641
Exposure duration ≥16 years with obstructive ventilatory pattern	4/32 (12.5%)	
Active smokers with obstructive ventilatory pattern	3/26 (11.5%)	0.298
Active smokers without obstructive ventilatory pattern	1/26 (3.8%)	

Frequencies are shown as the number and percentage of subjects with certain variable.

\* Tested by chi square test.

No significant difference was found between the number of subjects with exposure duration ≥16 years with registered obstructive ventilator pattern and those with exposure ≤15 years with associated obstructive ventilator pattern (P=0.641). Also, there was no significant difference between active smokers with and without registered obstructive ventilator pattern (P=0.298). Table 9 gives an overview of job exposure matrices data among vineyard workers (qualitative matrix, intensity and frequency).

**Table 9.** Job exposure matrices data on respiratory hazards in examined vineyard workers

	(n=45)
Job exposure matrices data	
Qualitative job-exposure matrix	
Exposure to dust	45 (100%)
Exposure to gases/fumes/vapors	41 (91.1%)
Exposure to pesticides	45 (100%)
Matrix with exposure intensity	
Exposure to dust	/
low	
intermediate	28/45 (62.2%)
high	17/45 (37.8%)
Exposure to gases/fumes/vapors	
low	39/41 (95.1%)
intermediate	2/41 (4.9%)

high	/
Exposure to pesticides	
low	21/45 (46.7%)
intermediate	22/45 (48.9%)
high	2/45 (4.4%)
Matrix with exposure frequency	
Exposure to dust	
rare	/
occasional	12/45 (26.7%)
regular	33/45 (73.3%)
Exposure to gases/fumes/vapors	
rare	25/41 (60.9%)
occasional	16/41 (39.1)
regular	/
Exposure to pesticides	
rare	22/45 (48.9%)
occasional	22/45 (48.9%)
Regular	1/45 (2.2%)

Frequencies are shown as the number and percentage of subjects with certain variable.

According to the data obtained by job-exposure matrices, almost all vineyard workers were exposed to the listed occupational respiratory hazards. In terms of exposure intensity, the majority were exposed to an intermediate level of dust and a low and intermediate level of exposure to gases/fumes/vapors and pesticides. In terms of exposure frequency, the majority of vineyard workers were regularly exposed to dust and rarely and occasionally to gases/fumes/vapors and pesticides.

## Discussion

Numerous studies conducted over the past few decades have shown a significantly higher risk of respiratory morbidity and mortality among agricultural workers, demonstrating a link between respiratory hazards in agriculture and the development of chronic respiratory symptoms, as well as chronic lung diseases<sup>[3]</sup>. The data obtained in the current study show that the most common work activities of vineyard workers included: digging, planting and weeding, watering, harvesting grapes and transporting them to the wineries, pruning vineyards in winter, plowing the soil to loosen it and uncover the base of the vineyards, their flowering and pruning of vineyards to obtain grapes in summer, cleaning work areas, etc. Their occupational exposure included unfavorable microclimatic conditions, dust, chemical hazards and pesticides, contact with plants, etc. This article delves into the factors affecting respiratory health among vineyard workers, the potential consequences on lung function, and the importance of preventive strategies to mitigate these risks.

The current study evaluated chronic respiratory symptoms and pulmonary ventilation in a group of vineyard workers. The average length of exposure at the current workplace among respondents was about 23 years, with over 70% of them having an exposure experience equal to or greater than 15 years. A relatively high prevalence of active smokers (about 57%) was registered among vineyard workers, which is somewhat higher than that in the previous research by Stoleski et al. among agricultural workers<sup>[20-22]</sup>. The largest number of vineyard workers, who were active smokers, had a smoking experience of 11-20 years and smoked 11-20 cigarettes during the day, while the frequency of passive and former smokers was 15.5% and 20%, respectively.

Many epidemiological and clinical studies indicate a higher prevalence of chronic respiratory symptoms and pulmonary ventilation disorders in agricultural and especially vineyard workers compared to other professions. The prevalence of people with chronic respiratory symptoms in the current study among vineyard workers was 44.4%, and about 20% of them indicated a work-related deterioration. The results indicated a higher frequency of cough (40%), cough with phlegm (31.1%), as well as dyspnea and wheezing (22.2%). In the study by Minov *et al.* (71) including workers engaged in the production of fruit teas, the prevalence of people with respiratory symptoms was 44.8%, compared to 33.6% in CG, and a significant difference was found for cough with phlegm and dyspnea.

According to studies across Europe, the prevalence of chronic respiratory symptoms varies from 25% to 35%<sup>[23]</sup>, while according to the study by Stoleski et al. comprising agricultural workers in the Skopje region, it was 26.6%<sup>[20]</sup>. The prevalence of cough with phlegm among farmers in the aforementioned study was 8.3%, which is similar to some previous studies in our country dedicated to respiratory effects caused by specific occupational exposure among agricultural workers<sup>[24]</sup>. A study in Poland that investigated grain growers showed a prevalence of 44.7% for chronic respiratory symptoms, and the highest rates were registered for chronic cough (26.3%) and dyspnea (19.7%)<sup>[25]</sup>. Many other studies also confirm the high prevalence of wheezing among agricultural workers compared to office workers<sup>[26]</sup>. Stoleski *et al.*<sup>[20]</sup> found a higher prevalence of total chronic respiratory symptoms in agricultural workers compared to office workers, with a significant difference for cough and wheezing. The prevalence of total respiratory symptoms in the study by Stoleski *et al.* analyzing the impact of smoking and the duration of occupational exposure on respiratory symptoms and functional lung disorders in agricultural workers<sup>[22]</sup> was 29.3%. Cough was present in 20%, cough with phlegm in 10.7%, while the prevalences of dyspnea, wheezing and chest tightness were 12%, 10.7% and 8%, respectively. In this regard, the study by Danuser *et al.* involving farmers in Switzerland, concluded that agricultural work was closely associated with the risk of developing chronic bronchitis (two times higher risk) and a four and a half times higher risk of cough with expectoration compared to the general population<sup>[27]</sup>.

The risk of respiratory symptoms in the current study was about two times higher in subjects with an exposure period of more than 15 years compared to exposed subjects with a shorter exposure period. The risk of respiratory symptoms was about three times higher in exposed subjects who were active smokers compared to exposed subjects who did not smoke. The length of smoking period and the number of cigarettes consumed during the day significantly affect the occurrence of respiratory symptoms in the studied winegrowers. A significant association of the length of exposure period with chronic bronchitis was also registered in the study by Omland *et al.* with 1691 farmers exposed to dust of plant and animal origin<sup>[28]</sup>. Chronic respiratory symptoms in agricultural workers in the study by Stoleski *et al.*<sup>[20]</sup> were significantly associated with the length of occupational exposure of more than 20 years, age over 60 years, exposure to chemical hazards, as well as the smoking habit in men. Many studies indicate a higher frequency of chronic respiratory symptoms in agricultural workers with longer-term occupational exposure, while those examining the respiratory effects of different types of organic dust report a significant association between smoking habits and chronic respiratory symptoms<sup>[29]</sup>. Research among farmers in France showed a synergistic effect of occupational exposure and smoking, especially for chronic cough and cough with expectoration<sup>[30]</sup>. In the study by Stoleski *et al.*, the frequency of active smokers among agricultural workers was 26.7%, and the frequency of respiratory symptoms in the last 12 months was higher in agricultural workers with exposure longer than 15 years, but with established

statistical significance only for overall respiratory symptoms and dyspnea<sup>[22]</sup>. The results of the current study indicate that the majority of subjects (about 80%) had preserved pulmonary ventilation with preserved or slightly reduced small airway flow. Some type of ventilatory insufficiency was recorded in about 20% of vineyard workers. The average values of spirometric parameters in winegrowers with an exposure experience of more than 15 years were lower than those in vineyard workers with an exposure experience of less than 15 years, with a statistically significant difference in small airway flow (MEF50, MEF75 and MEF25-75). Similar results have been obtained in many studies worldwide, also indicating reduced small airway airflow without associated respiratory symptoms, which confirms the fact that impaired small airway flow is the earliest sign of respiratory disorder<sup>[31]</sup>. Stoleski et al. in a survey of agricultural workers in rural areas showed that respiratory diseases during a year were among the most common, with a prevalence of 23.8%<sup>[20]</sup>.

A study by Stoleski *et al.* among agricultural workers in the Skopje region showed lower mean values of all spirometric parameters compared to a control group of office workers, with a statistically significant difference in mean values of MEF50 and MEF75. A combined pattern of ventilatory insufficiency predominated among agricultural workers, while ventilatory impairments were associated with age over 60 years, length of occupational exposure over 20 years, smoking habit and exposure to dust and pesticides<sup>[20]</sup>. Our previous study, which evaluated the COPD prevalence and characteristics among working population, showed that the most common respiratory symptoms among working population subjects with COPD were dyspnea (85.1%) and cough with phlegm (75.6%), while the mean post-bronchodilator values of basic spirometric parameters in exposed workers with COPD were significantly lower compared to mean post-bronchodilator values of basic spirometric parameters in non-exposed workers with COPD<sup>[32,33]</sup>. Furthermore, Stoleski et al. showed that the frequency of COPD among exposed retired smokers (12.6%) was significantly higher than its frequency among unexposed retired non-smokers (6.4%) ( $P=0.018$ )<sup>[34]</sup>. On the other hand, a study by Dosman *et al.*<sup>[35]</sup>, examining the effect of specific occupational exposure on the frequency of chronic respiratory symptoms and the decrease in functional lung parameters in workers engaged in cereal cultivation in Denmark, recorded significantly lower values of all spirometric parameters (including small airways) compared to the control group, and their decrease was significantly associated with age and pesticide exposure.

The current study found no statistically significant difference between the number of subjects with exposure experience  $\geq 16$  years with a registered obstructive pattern of ventilatory insufficiency compared to those with exposure  $\leq 15$  years with an associated obstructive pattern of ventilatory insufficiency. Also, there was no significant difference between active smokers with and without a registered obstructive pattern of ventilatory insufficiency. The study by Stoleski et al. demonstrated that ventilatory disorders in farmers were associated with age over 55 years, smoking habits and occupational exposure to dust, gases, vapors and pesticides longer than 25 years<sup>[21]</sup>, and another study by the same authors<sup>[22]</sup> confirmed the decline of functional lung parameters with the increase in the length of occupational exposure, but statistically significant only for MEF parameters in farmers who had been exposed for longer than 15 years.

Chen *et al.* in Canada suggested that there was a positive interaction effect between occupational exposure in grain farming and smoking habits on lung function and the prevalence of chronic bronchitis in women<sup>[36]</sup>. The study by Stoleski *et al.*<sup>[22]</sup> found a non-significant association between obstructive pattern of ventilatory insufficiency and active smoking, smoking history and number of cigarettes smoked in exposed agricultural workers, as well as the combined effect of length of exposure, smoking, smoking history and number of cigarettes smoked.

The study by Zuskin *et al.*<sup>[37]</sup> examined groups of grape growers and fruit growers from Croatia in order to determine the prevalence of respiratory symptoms and changes in lung function. The data showed that grape growers were prone to developing acute and/or chronic respiratory symptoms and changes in lung function, which were more pronounced in smokers. Changes in lung function in the studied workers were primarily related to FVC in smokers and non-smokers regardless of the duration of exposure. In grape growers exposed for more than 10 years, significant decreases in FEV1, MEF50 and MEF25 values were observed, which was attributed to the impact of pesticides. Exposure to pesticides in viticulture can cause asthma (new onset or exacerbation of existing), chronic obstructive pulmonary disease and even lung cancer. A large number of studies describe a variety of respiratory symptoms in agricultural workers exposed to pesticides. Hashemi *et al.*<sup>[38]</sup>, in a study of work-related symptoms in Iranian farmers, reported that pesticide use was associated with an increased risk of dyspnea. A study of grain farmers in Ohio found that pesticide use was associated with an increased incidence of chronic cough<sup>[39]</sup>. A case-control study of agricultural workers in India found that, compared to controls, agricultural workers who sprayed organophosphorus and carbamate pesticides had significantly lower erythrocyte acetylcholinesterase levels, which were significantly associated with almost all respiratory symptoms<sup>[40]</sup>. Hoppin *et al.* found that exposure to organochlorine and organophosphorus pesticides was significantly associated with dyspnea in commercial pesticide applicators after adjusting for age, BMI, smoking, presence of asthma/atopy, and previous pesticide use<sup>[41]</sup>.

In terms of pesticide use and lung function, a cross-sectional study of pesticide processing workers found that there were significant decreases in FVC, FEV1, and MEF25-75% relative to controls<sup>[42]</sup>. A similar study of pesticide sprayers in Spain suggested that short-term exposure to pesticides was associated with a decrease in FEV1, while long-term exposure was associated with a decrease in MEF25-75%<sup>[43]</sup>. Peiris-John *et al.*<sup>[44]</sup> studying farm workers in Sri Lanka found that organophosphate insecticides were associated with a decrease in FEV1 and FVC. In a case-control study of farm workers in India, exposure to organophosphate and carbamate insecticides was significantly associated with a decrease in FVC, FEV1, FEV1/FVC, MEF25-75%, and peak expiratory flow rate (PEFR), which was also significantly associated with cholinesterase inhibition<sup>[40]</sup>.

A study of work-related respiratory symptoms<sup>[45]</sup> reported a prevalence of work-related rhinitis of 6% and pulmonary symptoms of 3% in a large group of vineyard workers in France, associated with a higher rate of sensitization, but not with grape pollen, with symptoms occurring mainly in late spring. The prevalence of rhinitis and respiratory symptoms was 19% and 8%, respectively, and is similar to a study reporting rhinitis in 25% and asthma in 6% of the general population in France<sup>[46]</sup>. Spiewak *et al.*<sup>[47]</sup> described occupational rhinitis in 16% and cough and dyspnea in 9% of agricultural workers. A study of vineyard workers in Greece showed that grape growing was a risk factor for the development of occupational rhinitis, as well as cough and dyspnea<sup>[48]</sup>. A French study found an association between the frequency and severity of symptoms and sensitization to pollens and dust mites. Sensitization to grape pollen was reported in 14% of subjects, compared to a previous study in grape pickers and processors that found a prevalence of 3.7%<sup>[45]</sup>. A study of agricultural workers exposed to organophosphorus pesticides in North India<sup>[49]</sup> found that respiratory symptoms were significantly more common among pesticide sprayers, and that the duration of exposure increased with increasing frequency and severity of respiratory symptoms. The Iowa Family Farm Study found a clear association between pesticide use and respiratory symptoms, similar to the Ohio study that found pesticide use among grape and fruit growers was significantly associated with chronic cough<sup>[50]</sup>.

Among the studied group of vineyard workers, the exposure to occupational respiratory hazards (dusts, gases, fumes, vapors, pesticides) was assessed according to the matrices for occupational exposure to respiratory hazards. In terms of exposure intensity, the majority were exposed to a medium level of exposure to dust and to a low and medium level of exposure to gases/fumes/vapors and pesticides. In terms of exposure frequency, the majority of vineyard workers were regularly exposed to dust and rarely and occasionally to gases/fumes/vapors and pesticides. The study by Kauffmann *et al.* dedicated to the exposure to chemical hazards among agricultural workers showed that with the help of the matrices it was possible to make a quantitative assessment of the cumulative exposure of the respondents, but also to propose preventive measures for the prevention and early detection of respiratory disorders<sup>[51]</sup>. The French PAARC (Pollution Atmosphérique et Affections Respiratoires Chroniques) study found an association between dusts, gases and fumes and respiratory symptoms in both genders and the FEV1/FVC% ratio in men, as well as a significant association between known risk factors and a decrease in FEV1<sup>[52]</sup>. In a study on the potential of the occupational exposure matrix in detecting workplace risk factors for COPD, Le Moual *et al.*<sup>[53]</sup> indicated an association between estimated occupational exposure and impaired lung function. Matrices have been widely used to assess occupational exposure in larger groups of subjects, especially in cases where detailed questionnaires, environmental monitoring or expert assessment are lacking. Therefore, further research is needed to improve their performance and predictive value, to determine their association with specific occupational exposures in agriculture, to implement protocols for their evaluation, and to emphasize prevention strategies<sup>[3]</sup>.

This study has certain limitations. Specifically, the relatively small number of subjects in the study group, which was due to early termination of data collection caused by the onset of Covid-19 pandemic, and the lack of a control group and ambient monitoring could aggravate a clear relationship between occupational exposure and respiratory impairment among vineyard workers. Also, the absence of skin prick testing to common and workplace allergens could aggravate clear relationship between allergen sensitization and respiratory symptoms, as well as lung function parameters.

## Conclusion

A high prevalence of respiratory symptoms and lung function impairments were registered among the surveyed vineyard workers. The obtained results indicate the need of improving preventive measures to reduce work-related health risks among these workers. This knowledge should further contribute in detecting the critical points for action, and serve as a predictive factor in the development of respiratory diseases, within the diagnostic algorithm focused on respiratory health assessment. It also indicates the need for reduction of adverse occupational exposures through adequate preventive measures, regular health examinations, obligatory use of respiratory protective equipment, and implementation of engineering controls, together with counseling for smoking cessation.

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