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Asthma and Chronic Obstructive Pulmonary Disease Associated With Occupational Exposure in Dairy Farmers - Importance of Job Exposure Matrices

Saso Stoleski*, Jordan Minov, Jovanka Karadzinska-Bislimovska, Dragan Mijakoski, Aneta Atanasovska, Dragana Bislimovska

Institute for Occupational Health of Republic of Macedonia, WHO Collaborating Center, Ga^2len Collaborating Center, Skopje, Republic of Macedonia

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***Correspondence:** Saso Stoleski. Institute for Occupational Health of the Republic of Macedonia, WHO Collaborating Center, Ga^2len Collaborating Center, Skopje, Republic of Macedonia. E-mail: sstoleski@yahoo.com

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Abstract

AIM: To evaluate the prevalence of chronic respiratory symptoms, lung function impairment, and chronic obstructive respiratory diseases in dairy farmers. Our objective is to then examine their relation to exposure duration and to explore the usefulness of job exposure matrices as tools for exposure assessment, and predictors for respiratory health impairment.

METHODS: A cross-sectional study was performed, including 83 dairy farmers (mean age: 52.6 ± 8.7 years; mean exposure duration: 23.7 ± 7.6 years) and 80 office workers as a control group (mean age: 52.7 ± 8.2 years) matched for age, smoking habits, and socioeconomic status. Methods of evaluating examined subjects included a questionnaire on respiratory symptoms in the last 12 months, spirometry and histamine challenge, as well as the use of job exposure matrices (JEM).

RESULTS: Dairy farmers had a significantly higher prevalence of cough (38.5), phlegm (27.7%), and wheezing (21.7%), than controls ($p < 0.05$). All mean baseline spirometric parameters were lower in dairy farmers compared to the controls, but statistical significance was confirmed only for MEF25, MEF50, and MEF75% ($p = 0.010$, $p = 0.001$, and $p = 0.004$, respectively). The prevalence of bronchial hyperresponsiveness, asthma, and chronic obstructive pulmonary disease was higher in dairy farmers but without statistical significance. JEM were useful tools for exposure assessment and predictors of factors for asthma and COPD development.

CONCLUSION: The results suggest that occupational exposure among crop farmers is associated with a higher prevalence of respiratory symptoms, lung function impairment, and a higher prevalence of chronic respiratory diseases. JEM showed good potential for farming exposure evaluation and promoted their applicability within the diagnostic algorithm focused on respiratory health assessment.

Introduction

Lung diseases have been recognised among dairy farmers for decades. Studies of dairy farmers worldwide have shown increased rates of chronic bronchitis, chronic obstructive pulmonary disease (COPD), and asthma. Researchers have consistently reported the presence of chronic obstructive lung diseases, with decreased flows, bronchial hyperresponsiveness (BHR), and increased symptoms of wheezing, cough, and phlegm production [1], [2], [3], [4], [5], [6], [7].

Work on dairy farms has been associated with adverse respiratory symptoms, primary symptoms of bronchoconstriction, and decreased pulmonary function [4], [8], [9], [10], [11]. Dairy farmers may be at risk for lung inflammation due to the proximity of aerosol sources (e.g., cows) and exposure duration. Additionally, dairy farm workers often work long shifts for more than 5 days a week performing the same or similar tasks (e.g., milking) [12]. These aerosols may contain a mixture of manure, animal dander, hair, animal feed, gram-positive (muramic acid), and gram-negative (endotoxins) microbiological components [10].

Chronic airway diseases developing from exposure to large animal-feeding operations include a spectrum of upper and lower respiratory tract disorders: rhinitis, mucous membrane inflammation syndrome, sinusitis, asthma, asthma-like syndrome, chronic bronchitis, COPD, hypersensitivity pneumonitis and organic dust toxic syndrome (ODTS) [13], [14]. These diseases commonly occur following exposure to large animal feeding operation farming environments, particularly swine confinement facilities and commercial cattle feedlots [15].

Asthma is associated with large animal farming exposures. It is now well-recognised that children raised on farms have less allergic, IgE-mediated asthma [16]. It was postulated that exposure to endotoxin or other bacterial components abundantly present in various farming environments leads to decreased IgE-mediated disease development [17], [18], which is also consistent with the hygiene hypothesis.

COPD is a major public health concern with increasing morbidity and mortality rates worldwide [19]. Although smoking is the main risk factor for the disease, 25 to 45% of COPD cases are non-smokers [20]. Occupational exposure could also be involved in the development of COPD [21]. Several studies have demonstrated that farmers are more likely to have respiratory symptoms than the general population, although fewer of them smoke [7]; in particular, FEV1 and FVC of dairy farmers decline faster than expected [1], [4].

One of the most important public health problems in farming is respiratory diseases. Having in mind that exposure to most of the respiratory hazards in this sector can be controlled and reduced work-related respiratory diseases subsequently in dairy farmers caused by these agents are potentially preventable [22], [23].

In the present study we have compared the prevalence of chronic respiratory symptoms, lung function impairment, and chronic obstructive respiratory diseases between dairy farmers and office workers, further examined its relation to exposure duration, and explored the usefulness of job exposure matrices as tools for exposure assessment in dairy farmers, and predictors for respiratory health impairment.

Subjects and Methods

Study design and setting

Cross-Sectional research was conducted in the Center for Respiratory Functional Diagnostics by the team from the Institute for Occupational Health, Skopje-WHO Collaborating Center for Occupational Health and GA2LEN Collaborating Center within the period September 2017 and February 2018.

Study Sample

The representative study sample was calculated by the software program PEPI 4.04, with 95% confidence level and confidence interval ± 5.

To achieve the necessary sample size (having in mind possible selection and response bias), we have taken a representative sample of 83 dairy farmers and 80 matched office controls in a large-scale agricultural enterprise.

Subjects

We have examined 83 subjects (mean age = 52.6 ± 8.7) employed as dairy farmers (mean duration of exposure 23.7 ± 7.6). They were engaged in dairy farming with main activities composed of preparation of fodder feeding and animal meals, milking, staying in the barn, preparation of straw, and haymaking, cattle raising, as well as taking care about milk hygiene and health of the animals. They were exposed to various respiratory agents: dust, inappropriate microclimate conditions, chemical hazards, vapours, gases, as well as to heavy manual work, animal contact, unfavourable body positions, and repetitive hand movements. Inclusion criteria for the examined group (EG): employed subjects with age range 18 to 64 years involved in dairy farming and exposed to at least one occupational respiratory hazard (dust, gases, fumes, and vapours).

Exclusion criteria for the examined group: subjects younger than 18 or older than 64 years, and subjects not engaged in dairy farming. To avoid selection bias and results' deviations, the study did not include subjects with exposure to respiratory hazards other than dairy farming.

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

Also, a 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 for occupational exposure to respiratory hazards.

The subjects in both groups who were diagnosed by a physician to have some chronic respiratory disorder (asthma, COPD, bronchiectasis, sarcoidosis, etc.), or treated with bronchodilators and corticosteroids were not included in the study. Also, both groups did not comprise any subjects in whom either spirometry or bronchodilator reversibility testing was contraindicated.

All study subjects were informed about the study and gave their written consent accordingly.

The Institute's ethics committee has approved the content of our study protocol, whereas each examined subject was informed and gave written consent before any involvement in the study.

Questionnaire

All study subjects were interviewed by a physician and completed the standardised 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 [24], [25].

Classification of smoking status was done according to the World Health Organization (WHO) guidelines on definitions of smoking status [26].

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 [27].

Ex-smoker was defined as a formerly daily smoker, 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 [28].

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 for Coal and Steel (ECCS) norms. The spirometry results were given as percents of their predicted values due to the current European Respiratory Society (ERS) and American Thoracic Society (ATS) recommendations, including reproducibility and acceptability [29].

Histamine challenge

BHR was assessed by the histamine challenge test performed according to the actual European Respiratory Society (ERS)/American Thoracic Society (ATS) recommendations [30], [31]. Namely, concentrations of 0.5, 1, 2, 4, and 8 mg/mL histamine (Torlak, Serbia) were prepared by dilution with buffered saline. Afterwards, the doses of aerosol generated by Pari LC nebuliser with an output rate of 0.17 mL/min were inhaled by the mouthpiece. Subjects inhaled increasing concentrations of histamine using a tidal breathing method until FEV_1 fell by more than 20% of its base value (provocative concentration 20-PC_{20}) or until the highest concentration was reached.

According to the ATS recommendations, BHR was categorized as moderate to severe BHR ($PC_{20} < 1.0$ mg/mL), mild BHR ($PC_{20} = 1.0 - 4.0$ mg/mL) and borderline BHR ($PC_{20} = 4.0 - 8.0$ mg/mL) [31].

Job exposure matrices

To assess occupational exposure to respiratory agents among dairy farmers, we have 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 [32].

Diagnostic criteria for asthma and COPD

According to the actual recommendations by Global Initiative for Asthma (GINA), asthma in subjects with normal spirometry findings is defined as symptomatic BHR with $PC_{20} \leq 4$ mg/mL, whereas in subject with respiratory impairment with positive bronchodilator test [33].

According to the actual recommendations by Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD is defined by post-bronchodilator FEV_1/FVC ratio lower than 0.70 in subjects with dyspnea, chronic cough and/or cough with phlegm [34].

Statistical analysis

We have analysed the data 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

Table 1 gives an overview of the overall and demographic characteristics of the study subjects.

Table 1: Demographics of the study subjects

Variable	Dairy farmers (n = 83)	Office workers (n = 80)
Gender / M/F ratio	2.6	2.7
Age range (years)	20 - 63	21 - 64
Age (years)	52.6 ± 8.7	52.7 ± 8.2
BMI (kg/m^2)	25.4 ± 3.6	26.2 ± 3.7
Duration of employment (years)	26.3 ± 10.1	25.3 ± 9.8
Duration of exposure	23.7 ± 7.6	/
Daily smokers	39 (46.9%)	39 (48.7%)
Life-time smoking (years)	18.9 ± 7.6	19.2 ± 7.8
Cigarettes / day	14.6 ± 6.8	14.8 ± 7.2
Pack-years smoked	12.5 ± 4.8	12.9 ± 4.9
Ex-smokers	9 (10.8%)	12 (15%)
Passive smokers	7 (14%)	8 (16%)

Numerical data are expressed as mean value with standard deviation; frequencies as number and percentage of study subjects with certain variable; BMI: body mass index; kg: kilogram; m: meter.

The subjects of examined and the control group reported 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.

The frequency of chronic respiratory symptoms in the last 12 months is higher in dairy farmers compared to office controls, with a significant difference for cough, cough with phlegm, and wheezing (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 last 12 months in both examined groups and prevalence of respiratory symptoms in the last 12 months in dairy farmers with a duration of workplace exposure more and less than 20 years

Respiratory symptoms in the last 12 months	Dairy farmers (n = 83)	Office workers (n = 80)	P-value*
Any respiratory symptom	34 (40.9%)	23 (21.2%)	0.102
Cough	32 (38.5%)	17 (24.3%)	0.016
Phlegm	23 (27.7%)	12 (15%)	0.048
Dyspnea	17 (20.5%)	8 (10%)	0.063
Wheezing	18 (21.7%)	8 (10%)	0.041
Chest tightness	8 (9.6%)	6 (7.5)	0.626
Dairy farmers			
Respiratory symptoms in the last 12 months	Exposed > 20 years (n = 59)	Exposed ≤ 20 years (n = 24)	P-value*
Any respiratory symptom	32 (54.2%)	6 (25%)	0.015
Cough	27 (45.7%)	5 (20.8%)	0.034
Phlegm	19 (32.2%)	4 (16.7%)	0.151
Dyspnea	14 (23.7%)	3 (12.5%)	0.370
Wheezing	14 (23.7%)	4 (16.7%)	0.479
Chest tightness	5 (10.1%)	2 (8.3%)	0.983

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

The risk for development of chronic respiratory symptoms is about six-fold higher among dairy farmers exposed more than 20 years compared to those with shorter job exposure (OR = 5.93 (1.63-23.51) CI 95%).

The mean values of spirometric parameters are lower in dairy farmers compared to controls, but being significant only for MEF_{25}, MEF_{50}, and MEF_{75} (Table 3).

Table 3 shows the mean values of spirometric parameters in dairy farmers with an exposure duration of more than 20 years and those with less than 20 years.

Table 3: Mean values of spirometric parameters in examined groups and mean values of spirometric parameters in dairy farmers with a duration of workplace exposure more and less than 20 years

Spirometric parameter	Dairy farmers (n = 83)	Office workers (n = 80)	*P*-value*
FVC (% pred)	93.1 ± 9.6	94.3 ± 9.9	0.427
FEV_1 (% pred)	86.2 ± 8.8	87.2 ± 8.9	0.466
FEV_1/FVC%	73.4 ± 4.9	74.9 ± 5.1	0.054
MEF_{25} (% pred)	57.9 ± 7.1	60.7 ± 6.9	0.010
MEF_{50} (% pred)	58.2 ± 7.2	61.9 ± 7.1	0.001
MEF_{75} (% pred)	59.2 ± 6.7	62.3 ± 7.2	0.004
MEF_{25-75} (% pred)	61.9 ± 7.9	64.2 ± 8.3	0.068
Dairy farmers			
Spirometric parameter	Exposed > 20 years (n = 59)	Exposed ≤ 20 years (n = 24)	*P*-value*
FVC (% pred)	92.2 ± 9.4	94.1 ± 9.9	0.400
FEV_1 (% pred)	85.3 ± 8.4	86.7 ± 9.1	0.503
FEV_1/FVC%	72.2 ± 5.1	74.3 ± 4.8	0.087
MEF_{25} (% pred)	57.1 ± 6.9	58.2 ± 7.3	0.519
MEF_{50} (% pred)	56.5 ± 7.2	59.9 ± 6.7	0.050
MEF_{75} (% pred)	57.7 ± 6.9	61.1 ± 7.1	0.046
MEF_{25-75} (%pred)	60.3 ± 7.1	61.9 ± 7.9	0.370

Data are expressed as mean value with standard deviation. FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 second; MEF_{50}, MEF_{75}, MEF_{25-75}: maximal expiratory flow at 50%, 75%, and 25-75% of FVC, respectively; % pred: % of predicted value; * Tested by independent-sample *T*-test.

The mean values of spirometric parameters among dairy farmers exposed more than 20 years are lower than in those with exposure less than 20 years with a significant difference for MEF_{50} and MEF_{75}.

Table 4 gives an overview of the overall status of the EG and CG subjects concerning the presence or absence of some chronic respiratory disease.

Table 4: Frequency of asthma and COPD among study subjects

	Dairy farmers (n = 83)	Office workers (n = 80)	P-value*
No disease n (%)	56 (67.5%)	67 (83.7%)	P > 0.05
COPD n (%)	7 (8.4%)	3 (3.8%)	P > 0.05
Asthma n (%)	6 (7.2%)	4 (5%)	P > 0.05
Chronic bronchitis n (%)	14 (16.9%)	6 (7.5%)	P > 0.05

Data are given as a number and per cent of study subjects with a certain variable.

The effect of job exposure, among EG subjects, is assessed by their exposure to a certain respiratory hazard, and by their daily work activities. It is assessed as exposure to every hazard individually, but also as a combination of exposure to several respiratory hazards simultaneously. Furthermore, 83 dairy farmers are responsible for work in barns and other confinement spaces, working as cow breeders. Their daily activities include milking, animal feeding, mechanisation use, indoor and outdoor cleaning etc.

During daily activities, they are exposed to a wide spectrum of respiratory hazards such as dust, temperature variations, fodder, gases, vapours, moisture, fumes etc.

Distribution of chronic respiratory symptoms associated with exposure to respiratory hazards, analysed by the qualitative job-exposure matrix in dairy farmers is shown in Table 5 through the odds ratios, after adjustment for age, gender, and smoking habit.

Table 5: Frequency of chronic respiratory symptoms associated with exposure to respiratory agents in dairy farmers (Prevalence ORs (95% CI)*)

Data from job exposure matrices	Cough	Cough with phlegm	Chronic bronchitis	Dyspnea	Wheezing	Chest tightness
Qualitative matrix						
Exposure to dust	2.45 * (0.56-5.04)	1.41 (0.12-3.25)	3.21 * (0.67-9.14)	1.54 (0.33-3.36)	2.37 * (0.28-5.09)	1.78 (0.32-3.76)
Exposure to gases/fumes/vapors	1.42 (0.24-3.47)	3.04 * (0.47-7.12)	2.25 * (0.42-5.09)	2.73 * (0.42-4.48)	1.76 (0.21-3.87)	1.43 (0.17-3.51)

Data are given as odds ratios (ORs) with 95% confidence interval (95% CI); * P < 0.05; OR = odds ratio; CI: confidence interval; * Tested by logistic regression after adjustment for age, gender, and smoking habit.

According to the table exposure to dust significantly increases the risk for cough, chronic bronchitis, and wheezing, while exposure to gases/fumes/vapours has a significant influence on the cough with phlegm, chronic bronchitis, and dyspnea among dairy farmers.

Table 6 gives an overview of exposure to respiratory hazards according to the job exposure matrices among dairy farmers, related to the registered chronic respiratory diseases (asthma, COPD, and chronic bronchitis).

Table 6: Exposure to respiratory hazards according to job exposure matrices related to chronic respiratory diseases in dairy farmers

	No disease N (%)	COPD N (%)	Asthma N (%)	Chronic bronchitis N (%)	P-value*
Subjects n (%)	56 (67.5%)	7 (8.4%)	6 (7.2%)	14 (16.9%)	
Qualitative job-exposure matrix					
Dust	37 (66.1%)	6 (85.7%)	5 (83.3%)	12 (85.7%)	P > 0.05
Gases/fumes/vapors	33 (58.9%)	5 (71.4%)	5 (83.3%)	11 (78.6%)	P > 0.05
Matrix with exposure intensity					
Dust exposure					
Low	26 (70.3%)	0	0	2 (16.7%)	/
Intermediate	7 (18.9%)	2 (33,3%)	1 (20%)	3 (25%)	P > 0.05
High	4 (10.8%)	4 (66,7%)	4 (80%)	7 (58.3%)	P < 0.05*
Gases/fumes/vapors exposure					
Low	24 (72.7%)	1 (20%)	0	2 (18.2%)	/
Intermediate	6 (18.2%)	1 (20%)	1 (20%)	2 (18.2%)	P > 0.05
High	3 (9.1%)	3 (60%)	4 (80%)	7 (63.6%)	P < 0.05*
Matrix with exposure frequency					
Dust exposure					
Rare	25 (67.6%)	0	0	3 (25%)	/
Sporadic	8 (21.6%)	3 (42,9%)	1 (20%)	2 (16.7%)	P > 0.05
Regular	4 (10.8%)	4 (57,1%)	4 (80%)	7 (58.3%)	P < 0.05*
Gases/fumes/vapors exposure					
Rare	26 (78.8%)	0	1 (20%)	3 (27.3%)	/
Sporadic	5 (15.2%)	2 (40%)	1 (20%)	1 (9.1%)	P < 0.05*
Regular	2 (6%)	3 (60%)	3 (60%)	7 (63.6%)	P < 0.05*

Level of statistical significance: *P < 0,05; * Tested by chi-square test or Fisher's exact test for trend.

According to the table, development of asthma, COPD and chronic bronchitis in dairy farmers is significantly associated with regular exposure to dust with a high level of intensity, and sporadic and regular exposure to gases, fumes and vapours with high exposure intensity.

Association of asthma and COPD with exposure to respiratory hazards verified by job exposure matrices among dairy farmers, and expressed through odds ratios after adjustment for age, gender, and smoking habit, is shown in Table 7.

Table 7: Risk for development of asthma and COPD due to occupational exposure to respiratory agents according to the matrices for job exposure among dairy farmers

	OR (95% CI)	
	Asthma	COPD
Qualitative job-exposure matrix		
Dust	1.83 (0.40-3.71)	1,91 (0,43-3,90)
Gases/fumes/vapors	1.68 (0.32-3.64)	1,74 (0,27-3,81)
Matrix with exposure intensity		
Dust exposure		
Low	1.57 (0,19-3,63)	1,68 (0,30-3,73)
Intermediate	1.69 (0,22-3,87)	2,07 * (1,03-4,15)
High	2.28 * (1,21-4,36)	3,12 * (1,45-6,35)
Gases/fumes/vapors exposure		
Low	1.59 (0,45-3,52)	1,61 (0,42-3,79)
Intermediate	1.82 (0,63-3,77)	1,81 (0,53-3,92)
High	2.67 * (1,23-5,12)	3,14 * (1,75-6,25)
Matrix with exposure frequency		
Dust exposure		
Rare	1.67 (0.44-3.12)	1.63 (0.43-3.12)
Sporadic	1.81 (0.61-3.56)	1.83 (0.49-3.88)
Regular	3.03 * (1.33-5.98)	2.47 * (1.26-5.29)
Gases/fumes/vapors exposure		
Rare	1.54 (0.27-3.02)	1.67 (0.39-3.12)
Sporadic	1,71 (0,44-3,12)	1.85 (0.48-3.33)
Regular	2,18 * (1,04-4,05)	2.46 * (1.25-5.17)

Data are given as odds ratios (ORs) with 95% confidence interval (95% CIs). * P < 0.05; OR = odds ratio; CI: confidence interval; * Tested by logistic regression after adjustment for age, and smoking habit.

According to the results in the table, a high level of dust and gases/fumes exposure regularly significantly increases the risk for asthma development among dairy farmers. On the other hand, intermediate and high level of regular dust exposure in dairy farmers significantly increases the risk for COPD development. Having in mind exposure to gases/fumes/vapours, the risk for COPD development is significantly associated with a high level of exposure regularly.

According to data obtained by job-exposure matrices, asthma, COPD and chronic bronchitis in dairy farmers are significantly related to the high intensity of dust exposure regularly, as well as high intensity of exposure to gases, fumes and vapours both on sporadic and regular basis.

Discussion

Chronic respiratory symptoms, functional lung impairment and respiratory disorders remain important clinical and public health issues for farmers worldwide [35].

The actual study compares the prevalence of chronic respiratory symptoms, lung function impairment and chronic obstructive respiratory diseases between dairy farmers and office workers, focusing on job exposure matrices as an effective tool for exposure assessment. The prevalence of chronic respiratory symptoms among dairy farmers in the actual study is 40.9%, and 65% of them report their work-relatedness, while office workers report the frequency of 21.2% and no workplace association. The prevalence is higher among exposed workers, and significant for cough, phlegm, and wheezing.

Several publications report on two cohorts of dairy farmers established in the Doubs region of France [1], [2], [36]. Gainet et al., reevaluated the original 1986 cohort after 12 years with 157 dairy farmers and 159 controls [37], whereas the original cohort included 250 dairy farmers and 250 controls [1]. Accelerated declines in FVC and FEV_1 were associated with age, smoking, and male gender. The authors concluded that dairy farming was associated with increased risk of lung disorders and that a relationship exists between cumulative exposure to organic dust and a decrease in blood oxygen saturation and respiratory function [37]. In 1999, Chaudemanche et al. reevaluated a Doubs cohort from 1994 and compared 215 dairy farmers with 110 controls [4]. Current FEV_1 was lower among dairy farmers than controls, and dairy farming was associated with an accelerated decline of FEV_1 and FEV_1/VC over time. Mounchetrou et al. conducted a 12-year follow-up of the 1994 cohort, reevaluating 219 dairy farmers [38]. The key findings of this study were that those working on “traditional” dairy farms stopped working on the farm earlier than those who worked on “modern” farms. Other predictors of early cessation of work were the presence of asthma or impaired lung function, and age at inclusion. In 2006, Thaon et al., performed another follow-up on this same cohort, including 219 dairy farmers, 130 non-dairy farmers, and 99 controls [39]. The increased decline in FEV_1 and FEV_1 / FVC was associated with handling animal feed and years of exposure [39]. These studies show a consistent excess of chronic bronchitis among dairy farmers, with a continuing decline in pulmonary function in this cohort over more than a decade. Rask-Andersen conducted a 12-year follow-up among 380 Swedish farmers, mostly dairy farmers, focusing on asthma [40]. Greater declines were seen in farmers with asthma and chronic bronchitis [40]. Eduard et al.’s study of Norwegian farmers included personal exposure assessment of participants who had undergone clinical evaluations [7] with 12% of participants being dairy farmers and showed that FEV_1 was significantly reduced for livestock farmers. Several studies measured pulmonary function with inhalation exposure assessment. COPD was associated with higher exposures to dust and endotoxin in the study by Monsó et al., about the European farmers [14]. The duration of feeding (foddering) was identified as a significant risk factor in the occurrence of farming-induced COPD [41].

Several researchers have confirmed an increased prevalence of self-reported adult-onset asthma among US dairy workers compared with rural controls [42]. Similar, but less-pronounced findings were observed in a population-based study of 2903 dairy workers from New Zealand [43]. In a 12-year follow-up study among 380 Swedish (mostly dairy) farmers, an increase in asthma prevalence was found that was considerably greater for dairy farmers (from 2% to 9%) compared with the general Swedish population (from 3% to 6%) [40]. A nested case-control study among 2000 farming apprentice’s and 400 rural controls showed that the new onset of asthma was associated with dairy production (OR = 2.5) [44]. In another study reevaluating symptoms in the French Doubs cohort of 219 dairy farmers, 130 other agricultural workers, and 99 controls, they observed an increased OR for indices of asthma (OR = 1.5-2.5, not significant) among dairy farmers compared with controls [39]. Results from the same cohort suggest the early cessation of work to be associated with the presence of asthma [38].

In a cross-sectional study of 4735 Norwegian farmers, dairy farmers were more likely to have COPD (OR = 1.30), and reduced FEV_1 compared with crop farmers [7]. The prevalence of COPD among dairy farmers was 13.5%. Farmers with atopy were more susceptible to developing COPD [7]. No significant difference in lung function was found in a cross-sectional analysis of farmers and non-farmers among 150 subjects from the USA with COPD [45]. Monsó et al. conducted a cross-sectional study of COPD among 105 European farmers working in animal confinement buildings [14]. Lung function was measured before and after work, and symptoms documented using questionnaires based on the European Community Respiratory Health Survey (ECHRS) [46]. Eighteen of the farmers (17%) had COPD (7 mild, 8 moderate, 3 severe), and 20 (19%) had a variability of over 10% during the work shift. The ECRHS reported that the highest risk of developing occupational asthma (OA) was registered in farmers (OR 2.6, CI 1.3 to 5.4) followed by agricultural workers (OR 1.8, CI 1.0 to 3.2) [7], [47]. In adult farmers, asthma symptoms are more likely regarded as work exacerbated asthma (WEA) as opposed to OA [7]. Subjects with moderate or severe asthma and/or subjects not receiving optimal treatment of their asthma may develop WEA when exposed to potential irritants such as dust, fumes and sprays. OA in 90% of the time is IgE-mediated to components, which include animal dander, storage mites, and cockroach [48], while only a small portion of cases is irritant-induced OA. Farmers and agricultural workers have increased risk of respiratory morbidity and mortality from chronic bronchitis and COPD. Eduard et al., [7] reviewed multiple studies from European farmers and found that Danish swine farmers had the highest prevalence of chronic bronchitis at 32%, compared to 28% in farmers that had swine and cattle. Farmers that did not raise any livestock displayed the lowest prevalence at 18.6% [15]. Also, livestock farmers and dairy farmers demonstrated significantly increased risk of developing COPD (livestock farmers, OR 1.4, CI: 1.1 to 1.7; dairy farmers, O.R.1.3, CI: 1.0 to 1.7) [7]. Moreover, raising more than one type of livestock enhanced the risk of farmers developing chronic bronchitis and COPD as compared to crop farmers. The livestock farmers also showed the lowest FEV_1, consistent with the pattern of lung function decline [7].

Agricultural workers inhalation exposure to dust measured over the work-shift has been reported from 0.8 to 20 mg per cubic meter (mg/m^3) [15], [10], [49]. As dairy production has increased in size due to the raising of economy, task-specialisation has increased [50]. However, little information is available on the characterisation of task-based exposures among dairy workers. Previous studies of inhalation exposure have combined exposure measurements across several tasks in dairy production (e.g., milking and feeding); consequently, limiting the application of the industrial hygiene hierarchy of exposure controls [51].

In the absence of detailed questionnaires, ambient monitoring or expert's evaluation, the exposure assessment using job exposure matrices can provide useful information within epidemiological studies [52].

Within the EG, the exposure to occupational respiratory hazards (dusts, gases, fumes, vapors) in each subject, besides through self-reported Questionnaire for occupational exposure to respiratory hazards, in the current research has also been estimated according to the data obtained from job exposure matrices to respiratory hazards (qualitative, matrix with exposure intensity, and matrix with exposure frequency). In this way, exposure to certain occupational respiratory hazards is also consistent with the specific work activities of the farmers, and it is possible to determine the predictive factors (qualitative or quantitative exposure to respiratory hazards) for the occurrence and development of chronic respiratory symptoms, as well as ventilatory impairment among the EG.

The results of our previous study recognised the role of job exposure matrices in farming exposure assessment and characterisation, their potential to be a predictive factor in the development of respiratory diseases, and promote their applicability within the diagnostic algorithm for respiratory health assessment among crop farmers [53].

Exposure to dust significantly increases the risk of cough, chronic bronchitis and wheezing, exposure to gases/fumes/vapours significantly affects the risk of cough with phlegm, chronic bronchitis and dyspnea, while exposure to gases/fumes/vapours significantly impacts the occurrence of dyspnea in the EG. The exposure intensity matrix gives an overview of the influence of the exposure degree to respiratory hazards (low, medium, high) on the occurrence of chronic respiratory symptoms, as well as the spirometric parameters in the EG subjects, while the exposure frequency matrix indicates it for the frequency of exposure to respiratory hazards (rarely, occasionally, regularly).

An Italian study dedicated to the exposure of chemical hazards in agricultural workers shows that with the help of matrices, it is possible to make a quantitative assessment of the cumulative exposure of the subjects, as well as to propose measures for preventing and early detection of respiratory disorders and workplace promotion of health workplace among agricultural workers [54]. The British matrix was applied in a study by Zutphen et al., [55] to explore the relationships between specific hazards and chronic non-specific lung disease, without associating with the lung function parameters. In the French study PAARC (Pollution Atmospheric et Affections Respiratoires Chroniques), an association was found between dust, gases, and fumes, and respiratory symptoms in both genders, and the FEV_1/FVC ratio in men. Examining the relationship between occupational exposures and pulmonary function, the study discovers a significant association of known risk factors and the FEV1 decline as evidence for the validity of matrices [56].

The asthma prevalence is associated with workplace exposure to dust, gases and fumes, estimated as self-reported or through an external job-exposure matrix [57]. A matrix specific for asthma was developed in the French epidemiological study dedicated to the association between genetic factors and the environment in asthma (EGEA) [58]. The study shows that the asthma risk associated with occupational exposure to specific high molecular weight agents can be identified using an asthma-specific job-exposure matrix.

According to the data from job exposure matrices in the current research, it was concluded that the occurrence of asthma, COPD and chronic bronchitis in EG subjects is significantly related only to regular and high-intensity exposure to dust, as well as occasional and regular exposure to gases, fumes and vapours with high exposure intensity.

Epidemiological studies in France, the Netherlands and Norway provide data on an individual basis for occupational exposure to respiratory hazards and lung function. Significant associations have been found between occupational exposure assessed by a specific job exposure matrix and pulmonary function in research in rural settlements in France and the Netherlands, but there is no significant relationship with self-reported exposure to respiratory hazards using a questionnaire [59].

Taking into account the matrices with the intensity and frequency of exposure in the current research, it can be concluded that the high level of exposure to dust and gases/fumes/vapours on a regular basis, significantly increases the risk of asthma in subjects from EG, and the medium and the high degree of regular exposure to dust significantly increases the risk of COPD. In terms of exposure to gases/fumes/vapours, the risk of developing COPD is significantly related to the high level of exposure regularly.

In our previous study about COPD in never-smoking dairy farmers, the results have shown that dairy farmers had a significant association between COPD and employment duration of over 20 years, but also between COPD and work-related chronic respiratory symptoms. The study findings are in line with the results from other similar studies about the cause-effect association between job exposure to respiratory hazards among dairy farmers and the development of persistent airway obstruction among dairy farmers [60].

In a study on the performance of the job-exposure matrix in detection of risk factors for the onset of COPD, Le Moual et al., [61] indicate the association between the estimated occupational exposure through the specific population matrix and impaired pulmonary function, unlike the so-called, self-reported exposure that has not revealed such a relationship in men or women in the French study, nor in a study in Denmark's rural areas. The study shows that job exposure matrices are relatively easy to design, their application is not limited to the number and categories of workers involved, and have much better performance than the self-reported method using questionnaires, especially when it comes to larger groups of respondents with similar work activities [61].

The job-exposure matrices for respiratory hazards in farmers provide an opportunity to evaluate occupational exposure by cross-summarizing the results for the types of activities and exposure to various hazards through several indicators (presence, intensity, frequency and/or probability), combining with data from work history and assessment of exposure during the total exposure duration period.

The matrices are widely used for assessing occupational exposure and for generating hypotheses in large groups of respondents, especially in the absence of specific questionnaires for occupational exposure. Despite the expected disadvantages, the matrices offer great opportunities and deserve a special place in the assessment of exposure to occupational respiratory hazards. Further research is needed to improve its performance and predictive value [56].

This study has certain limitations, namely, the relatively small number of subjects in the study groups, and an absence of ambient monitoring, which could aggravate a clear relationship between occupational exposure and respiratory impairment in dairy farmers.

In conclusion, our data revealed a higher prevalence of respiratory symptoms, significantly lower values of small airways indices, and a higher prevalence of asthma and COPD in dairy farmers compared to controls, also associated to exposure duration. The results recognised the role of job exposure matrices in assessment and characterisation of farming exposure, confirmed their potential to be a predictive factor in the development of respiratory diseases, and promote their applicability within the diagnostic algorithm focused on respiratory health assessment.

This knowledge should further contribute in the detection of critical points for action, but also indicate the need for reduction of adverse occupational exposures through adequate preventive measures, obligatory use of respiratory protective equipment, and implementation of engineering controls.

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