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A Cross Sectional Study of Respiratory and Allergy Status in Dairy Workers

Jose Carmona*,
Marine deMarcken*,
Pauline Trinh*,
Lauren Frisbie,
Vickie Ramirez,
Pablo Palmandez,
Sverre Vedal,
Coralynn Sack,
Peter Rabinowitz
Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington, USA

Abstract

Introduction: Workers on dairy farms face exposures to organic dusts and endotoxin. At the same time, a number of studies of farmers have reported a lower prevalence of asthma in farmworkers compared to persons without farm contact. The "hygiene hypothesis" suggests that early life exposures on farms could be protective against allergic disease and asthma. Such protective relationships are less well studied in adult farm workers.

Methods: A cross-sectional analysis of respiratory function and allergy status was performed in a sample of dairy farm workers (*n* = 42) and community controls (*n* = 40). Measures of respiratory status (spirometry, exhaled nitric oxide FeNO, self-reported symptoms) and levels of total and bovine-specific IgE were compared between the groups.

Results: Prevalence of self-reported asthma and most respiratory symptoms was similar in the two groups, with the exception of increased report of dyspnea among dairy workers. In the dairy workers, level of lung function was not reduced and FeNO was not increased. In unadjusted and adjusted models, dairy work was not associated with reduced lung function or increased airway inflammation. Mean IgE levels did not differ significantly between workers and controls, but elevated bovine-specific IgE was detected only among dairy workers, with an apparent association between elevated bovine IgE and increased FeNO.

CONTACT Vickie Ramirez, ramirezv@uw.edu, Department of Environmental and Occupational Health Sciences, Hans J. Rosling Center for Population Health Suite, University of Washington, 202/ Box 351618 3980 15th Avenue NE, Seattle, WA 9819, USA.
*authors contributed equally.

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Conclusion: While dairy workers did not demonstrate increased asthma prevalence compared to controls, sensitization to bovine antigen in several workers appeared to be associated with airway inflammation. Occupational health programs for dairy workers should consider the risk of animal allergy as part of respiratory health protection efforts.

Keywords

Dairy workers; occupational allergy; occupational asthma

Introduction

Workers on dairy farms are exposed to a variety of hazards including dusts and aerosols that could cause respiratory disease. Microbial components in organic dust, such as endotoxin, are known to have negative effects on lung health in livestock farmers due to their pro-inflammatory properties and together with airborne chemicals can have direct irritant effects.[1-3] The respiratory health of workers may also be impacted by exposure to animal dander and other allergens including bovine allergen, which over time may lead to allergic sensitization.[4] The trend towards larger animal agricultural operations has been associated with greater concentrations of many airborne exposures, indicating the need for ongoing assessment of possible effects on worker respiratory health.[5]

Despite this exposure to respiratory hazards, a number of studies have reported lower rates of allergy and asthma among people living on farms compared to the general population.[6] Some investigators have explained these findings by invoking the “hygiene hypothesis,” whereby exposure to dusts and microbes on farms may have a beneficial effect on immune function.[7,8] A number of these studies, for example, have reported lower levels of total serum immunoglobulin E (IgE), a measure of allergic sensitization, in children living on farms compared to community counterparts.[9] Although there are fewer studies in adults, there is some indication that the beneficial effect of farm exposure in childhood may persist later in life.[10]

A better understanding of the role of farm exposures in the development of allergy and asthma could enhance efforts in effective prevention of respiratory disease in farm workers.

We conducted a cross-sectional analysis of baseline findings within a larger longitudinal study to assess differences in respiratory status and allergic sensitization to bovine allergen between workers on dairy farms and community controls who did not work in dairy farming.

Methods

Population sample

The Healthy Dairy Worker study is a longitudinal health study of dairy workers and community controls. Subjects were recruited among workers on 3 large (>5000 Animals) dairy farms in the Yakima Valley of eastern Washington State, and community controls were recruited from surrounding communities. Recruitment of the community members as well as dairy worker subjects used a snowball sampling method (a non-probability sampling approach in which research participants identify other potential subjects). The study began initial enrollment of subjects in May 2017.

To be eligible for the study, dairy farmworker subjects had to have been working on a dairy farm for at least 6 months (dairy workers). To be eligible to be a community control, subjects had to have not worked on a dairy farm for at least the preceding five years, not be living on a dairy farm, and have no household member who worked on a dairy farm in the past five years. Oversampling of Hispanic or Latino males was conducted during recruitment of community controls to match the sex and race/ethnicity of the dairy workers. No other matching was performed during participant recruitment. Amongst the community control group, two individuals had retired and were not actively employed. Approximately 48% of control subjects identified as employed in plant agricultural industries. Study subjects received an incentive payment for baseline enrollment and during follow-up at 3, 6, 12, and 4 months. Following enrollment, baseline testing of subjects included a baseline questionnaire and lung function testing consisting of exhaled nitric oxide and spirometry performed by a trained technician. At the initial visit, blood was drawn for later analysis of total IgE and bovine specific IgE.

All procedures involving human subjects were reviewed and approved by the University of Washington Human Subjects Review Committee, STUDY00000042.

Questionnaire

A questionnaire regarding health status and occupational risk factors was modified and developed from an instrument used for previous studies of animal workers[11]. The updated questionnaire was pretested on dairy workers and community members by the interviewers administering the survey. The pretesting was an opportunity to test the questionnaire and make any necessary changes and adjustments. Prior to the pretesting the interviewers received training on administering the questionnaire by other research scientists at the University of Washington.

The revised survey was administered by trained interviewers in either English or Spanish according to subject preference. The interviewers administering the survey were bilingual, bicultural, and familiar with the community. The interviewers were fluent in Spanish and English.

The questionnaire included items about occupational tasks, respiratory symptoms at work and home, working history, smoking habits, family history, diet history and standard demographic questions. Respiratory symptoms were adapted from the ATS questionnaire, and included dyspnea, chest tightness, dry cough, and coughing with phlegm. Dyspnea was defined as shortness of breath when hurrying on level ground or walking up a slight hill, or shortness of breath when walking with someone of the same age on level ground.

Worker occupational exposures were characterized by responses to questions regarding job title, work tasks, number of hours worked per week for each task, amount of contact time with animals, exposures to dust, raw milk use, and other work details. Work tasks were divided into 3 categories: milker, maintenance work, or work with calves. The percent time of each task was calculated per worker based on the total number of hours currently working on the farm.

Spirometry

Lung function was measured using a portable spirometer (NDD Easyone_TM Plus Frontline Spirometer: EASYONE, Medical Technologies Inc., Andover, MA).

A nose clip was used during all spirometry measurements. Spirometry was measured on the subjects while in a seated position and instructions were given to each participant on the proper way to exhale into the equipment. The tests were performed according to guidelines from the National Institute for Occupational Safety and Health (NIOSH)[12]. Age, sex, height, and weight were recorded at each visit.

The following lung function parameters were measured during each visit, including the data from the best effort and the percent predicted[13] of the following: forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and ratio of FEV1/FVC. Measurements were taken every 30–0 seconds, with a maximum of 5 attempts per participant. The testing goal was to record three adequate maneuvers with less than 5% variability between these three best acceptable measurements. The study team performing testing were trained previously on how to conduct spirometry tests using OSHA’s Spirometry Testing in Occupational Health Programs guide[14] and a standard operating procedure was piloted prior to testing subjects. Spirometry was performed at times that were convenient for the subject; this included times before and after work hours and during days off from work.

Exhaled nitric oxide (eNO)

Subject level of exhaled nitric oxide (FeNO) was measured by a study team member following written protocols. The fraction Exhaled Nitric Oxide (FeNO) was assessed using a handheld device, NIOX VERO (Circassia Pharmaceuticals Inc, Chicago, IL). The FeNO test was performed prior to spirometry. Subjects were asked to refrain from eating and drinking for 1 h before the FeNO test. A short demonstration was played for the subject on a laptop computer screen to explain the proper method of blowing into the FeNO measuring instrument.

IgE

Serum samples for total IgE and bovine-specific IgE were drawn within several days of completion of the questionnaire and lung function testing. Blood was drawn by venipuncture by trained phlebotomists and centrifuged (0 min at 300 g at room temperature) within 4 h of collection. After centrifugation, serum was collected and placed in aliquot tubes that were frozen and kept at −80 degrees C until analysis.

Both total IgE and bovine-specific IgE were measured at University of Washington Department of Laboratory Medicine by radioaller-gosorbent assays (Phadia CAP System IgE FEIA for total IgE, ImmunoCAP System Specific IgE FEIA for IgE specific to cow epithelium (the most common bovine aeroallergen) and reported in units of antibody per milliliter (U/ml).

Data analysis

Study data were collected and managed using REDCap (Research Electronic Data Capture) tools hosted at University of Washington.[15,16] For the current analysis, data were abstracted for the baseline or study enrollment visit of each subject. This included results of spirometry, exhaled nitric oxide, the questionnaire data and total and bovine-specific IgE. Further data cleaning was performed in R Software version 3.6.1 using tidyverse packages. All missing entries from the REDCap download were treated as missing data and any duplicate entry was deleted. Potentially erroneous data entries in RedCap were corrected after careful review by study staff. Workers were given results of their lung function and IgE testing and those with abnormal results were counseled to consult with their medical provider.

Descriptive analysis included measures of central tendency and spread for continuous variables and frequencies of binary and categorical variables for key covariates. Single variable associations were analyzed using t-tests and chi-square. All descriptive analyses were performed using R version 3.6.1.

The two principal continuous outcomes of interest were FEV1% predicted and FeNO. FeNO was log-transformed because of skewness. Predictors of these outcomes were assessed using three separate analyses: 1) an unadjusted comparison of the outcomes between workers and community members, 2) a minimally adjusted model that included smoking, age, gender, race, height, BMI, and growing up on a farm as covariates, and 3) a fully adjusted model with additional covariates including reported raw milk consumption and total IgE level. Modeling was conducted using multivariable ordinary least squares regression. All multivariable analyses were conducted using the stats R-package, specifically the lm() function.

Results

Table 1 shows baseline demographics and risk factors for the dairy workers and the controls. Community control subjects were somewhat older and less likely to be current smokers. More of the farm workers were male and Hispanic compared to the controls. More than 10% of each group reported consuming raw milk in the past month. The majority of study participants grew up on a farm with a slightly higher percentage of workers reported growing up on a farm compared to community controls ($p = .092$).

Table 2 shows the results of spirometry and reported respiratory symptoms for both groups. While FEV1% predicted did not differ between the groups, FEV1/FVC ratio was higher among the workers compared to controls ($p = .011$). There were no significant differences between the two groups in FeNO or the percentage of persons with diagnosed asthma or most reported respiratory symptoms, with the exception of dyspnea, which was increased and only present in the dairy workers. There was no statistically significant association between job task and FeNO levels (data not shown). We additionally looked at differences in FeNO levels between those who were current smokers or had ever smoked compared to those who have never smoked and found no statistically significant differences between groups based on smoking status ($p = .54$).

Table 2 also shows the results of IgE testing for the two groups. Levels of total IgE were similar in dairy workers and controls. There was no association between principal job task and IgE levels (data not shown). There were suggestive differences, however, between workers and controls in the results of bovine specific IgE, with five of the workers exhibiting IgE levels above the 0.2 U/ml threshold, and four above the 0.5 U/ml threshold, while none of the community controls had bovine specific IgE above either cutoff.

Of the four workers with elevated bovine IgE above the 0.5 U/ml cutoff, two also had FeNO levels above 25ppb and one of these had FeNO>50ppb. Three out of these four dairy workers with elevated bovine IgE identified as current smokers. We found no evidence of a statistically significant association between smoking status and FeNO levels amongst these four dairy workers ($p = .29$).

Table 3 shows the results of bivariate and multivariate modeling for FEV1% of predicted. Neither dairy work status nor other risk factors were significantly associated with FEV1% of predicted in any model. Similarly, as shown in Table 3B, neither dairy work nor other risk factors significantly predicted log (FeNO) in any of the models.

Discussion

Despite evidence that certain exposures in dairy farming may have potential to cause lung inflammation and asthma, this cross-sectional study of dairy workers and community controls did not identify an elevated risk of asthma in workers. The assessments of respiratory status included symptom self-report, spirometry testing, and measurement of exhaled nitric oxide, an index of airway inflammation. There was no evidence that dairy worker exposures were associated with either reduced lung function or increased airway inflammation as reflected by FeNO. The FEV1/FVC ratio was higher in dairy workers compared to controls. However, dairy workers did report more dyspnea. Several dairy workers also had sensitization to bovine specific allergen, with no sensitization identified among the community controls. In addition, there was a suggestion that bovine sensitization was associated with airway inflammation since two of the workers had borderline or increased FeNO. These findings have relevance to the occupational health of dairy workers, in that steps to recognize and prevent allergic sensitization in such workers could reduce the risk of asthma or other allergic disease.

The lack of excess asthma among the dairy workers compared to community controls in this study is consistent with other reports suggesting a possible protective effect of exposure to farm environments against the development of allergies and asthma.[17] Such protective effects have been reported predominantly in children, and less is known about possible effects on adult workers such as the dairy workers in this study, some of whom had not grown up on farms. At the same time, the possibility of “selective survival”, with persons experiencing respiratory problems leaving the workforce at a greater rate, leaving behind a less susceptible group of workers, cannot be excluded in this cross-sectional analysis. Further longitudinal studies are needed to explore the role of selective survival in this workplace setting.

The finding of bovine-specific allergen reactivity in only the dairy workers and not among the controls suggests that there could be some risks for allergy and asthma in the dairy environment. This is consistent with findings from a small number of other studies of this problem. Cow dust was reported to be responsible for almost 40% of new occupational asthma cases in Finland. [17,18] Studies have shown that such allergy is related to cow dander and not to cow milk associated antigens.[18,19] Allergy to bovine dander has been seen in other cattle workers, such as cattle claw trimmers.[20] Studies have also found that there may be differences in bovine dander antigen across multiple cow breeds, implying a need to test workers with antigen tests derived from the specific breed they are working with.[21]

In our study, two of the four workers with bovine specific IgE levels above the 0.5 U/ml cutoff had evidence of airway inflammation reflected by an elevated FeNO. Screening for bovine allergy is not routine among dairy workers, but our findings suggest that health and safety programs targeting dairy workers should consider monitoring workers for development of allergies and exploring measures to reduce allergen exposure. Based on previous research, there may also be value in developing allergy tests for specific breeds of cows for use in screening workers exposed to those breeds.

The study has a number of limitations, including the cross-sectional design and the limited sample size. The use of snowball sampling to recruit participants may have also resulted in selection bias and affected the generalizability of our results. There were also some significant differences in demographics between the workers and community controls, although controlling for these differences did not alter the findings of a lack of elevated risk of asthma, decreased lung function, or increased airway inflammation among the dairy workers. Asthma is a complex and heterogeneous airway disease that can be caused by both allergic and irritant mechanisms. The protective effect as described by the hygiene hypothesis has been associated with protection against allergic asthma characterized by eosinophilic inflammation driven by a Th2 response and production of IgE.[22,23] In contrast, non-allergic asthma results from an inflammatory response to inhaled irritants that is not IgE-mediated and occurs in the absence of sensitization to an allergen. Whereas allergic asthma often develops in childhood, non-allergic asthma has a later onset. Our study design, including the reliance on self-reported asthma status and symptoms, did not allow us to distinguish between allergic and irritant-induced asthma. At the same time, the finding of higher FeNO levels in two of the four workers with elevated bovine IgE suggests that allergy may play at least a limited role in the respiratory status of the dairy workers in this study. We used a generic IgE test for bovine antigen that may have been less sensitive than a test developed using animal dander from the study locations. Furthermore, our spirometry measurements were collected at times that were convenient to subjects either before or after work shifts. The inconsistent timing of spirometry measurements relative to the work shift may influence our results as occupational studies have shown that workers experience cross-shift reductions in lung function measurements such as FEV1 and FVC[24-27]. Another limitation was the lack of information regarding environmental exposures to dust, CO_2 levels, and endotoxins. These environmental factors have been shown to impact non-allergic respiratory conditions[27] and potential similarities in exposure levels between groups may have influenced our study findings. Finally, approximately 48% of the community control group had reported employment in plant agricultural industries.

The similarities in occupational exposures between plant agriculture workers and dairy workers may have contributed to the null findings of our study. At the same time, study strengths included the use of objective measures of airway inflammation (FeNO) and allergy (IgE testing), and the use of community controls. While the present work focuses solely on the baseline characteristics of a longitudinal worker cohort, further analyses will investigate longitudinal trends in airway inflammation and allergic sensitization.

Conclusion

Host-environment interactions related to the respiratory health of dairy farm workers are complex and may involve both positive and negative effects of dairy farm exposures. Allergy to bovine antigens deserves greater attention in dairy farmworker health research and prevention. While the present study did not find evidence of increased risk for atopic allergic asthma in dairy workers, these null findings may be due in part to "selective survival" where workers with atopic asthma may have left the occupation due to dairy farming exposures. Additionally, we note that the community control group from our study consisted of many individuals employed in plant agricultural farming. Similar occupational exposures between agricultural and dairy farm workers may have contributed to the null findings of our study. Future studies are thereby warranted that utilize a control population from a workforce without similar occupational exposures i.e., office workers to confirm the lack of association between atopic allergic asthma and working on dairy farms. Detection of potential allergy risks could lead to early intervention and prevention of more serious consequences.

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Table 1.

Demographics and Risk factors.

	Dairy (N = 42)	Controls (N = 40)	P value
Age (mean, sd)	37.10 (7.10)	44.97 (13.54)	0.002
Sex (male)	97.6%	82.1%	0.072
Current Smoker	32.5%	17.1%	0.208
Grew up on a farm	88.1%	69.7%	0.092
Race/ethnicity			
White Hispanic	94.7%	68.6%	0.002
White non-Hispanic	0%	22.9%	
Other	5.3%	8.6%	
Drank raw milk in past 3 months	10.3%	14.7%	0.826
Years in Dairy Work	11.81 (7.12)	NA	-
Task: Milker, N %	17 (40.5%)	NA	-
Task: Maintenance, N %	24 (57.1%)	NA	-
Task: Works with Calves, N %	19 (45.2%)	NA	-

Table 2.

Respiratory and allergy status in dairy workers and controls.

	Dairy (N = 42)	Controls (N=40)	P value
FEV_1 % predicted (mean, sd)	91.14 (13.85)	90.22 (24.47)	0.835
FEV1%pPredicted<80 (N,%)	10 (23.8)	6 (15)	0.619
FEV_1/FVC ratio (mean, sd)	96.26 (6.84)	88.25 (18.65)	0.011
FEV_1/FVC<0.7 (N,%)	0	4 (10%)	0.09
Mean FeNO (sd)	18.54ppb (14.11)	20.68ppb (15.05)	0.525
FeNO 25–50 ppb	7 (16.7%)	7 (17.5%)	1
FeNO>50ppb	2 (4.7%)	2 (5%)	1
Asthma diagnosis (N,%)	4 (10%)	4 (11.8%)	1
Cough	5 (11.9%)	7 (17.5%)	0.686
Shortness of breath	9 (21.4)	0	0.006
Chest tightness	4 (9.5)	0	0.137
Mean total IgE U/ml (sd)	161.37 (204.75)	160.45 (230.12)	0.986
Positive bovine IgE (0.5 U/ml threshold) N (%)	4 (11.4%)	0	0.154
Positive Bovine IgE (0.2 U/ml threshold)	5 (14.3%)	0	0.085

Table 3a.

Regression models of FEV1% of predicted.

	Estimate	SE	p-value
unadjusted model			
dairy worker	−0.996	3.822	0.795
minimally adjusted model			
dairy worker	−1.1802	4.3125	0.785
current smoker	−5.0860	5.2084	0.332
ever smoker	0.8669	4.7721	0.856
grew up on a farm	8.5375	5.6302	0.134
fully adjusted model			
dairy worker	−2.008004	4.402378	0.650
current smoker	−1.053720	5.280617	0.843
ever smoker	3.896003	4.903115	0.430
grew up on a farm	−0.619492	6.031564	0.919
drank raw milk	−3.584138	5.785646	0.538
total IgE	0.002762	0.009068	0.762

Table 3b.

Regression models of log (FeNO).

	Estimate	SE	p-value
unadjusted model			
dairy worker	−0.107	0.144	0.460
minimally adjusted model			
dairy worker	−0.172	0.213	0.424
age	0.003	0.010	0.759
current smoker	−0.193	0.241	0.428
ever smoker	−0.102	0.222	0.649
male	0.199	0.430	0.647
white-hispanic	0.363	0.296	0.226
height	−0.026	0.034	0.445
bmi	−0.037	0.021	0.090
grew up on a farm	0.317	0.307	0.306
fully adjusted model			
dairy worker	−0.090	0.232	0.699
age	0.006	0.010	0.574
current smoker	0.019	0.264	0.942
ever smoker	−0.254	0.251	0.316
male	0.291	0.453	0.524
white-hispanic	0.302	0.318	0.347
height	−0.037	0.047	0.434
bmi	−0.037	0.023	0.120
grew up on a farm	0.339	0.335	0.317
drank raw milk	0.291	0.304	0.345
total IgE	0.001	0.000	0.219