Scientific Research Publishing

Health, 2024, 16, 1161-1175
https://www.scirp.org/journal/health
ISSN Online: 1949-5005
ISSN Print: 1949-4998

Examination of Respiratory Health-Consideration of Atopic and Non-Atopic Staff in Veterinary Practices

Frank Hoffmeyer[1], Alexandra Beine[1], Michal Gina[1], Eva Zahradnik[1], Olaf Kleinmüller[2], Ingrid Sander[1], Albert Nienhaus[2,3], Monika Raulf[1]

[1]Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-University Bochum (IPA), Bochum, Germany
[2]Competence Center for Epidemiology and Health Services Research for Healthcare Professionals (CVcare), Institute for Health Services Research in Dermatology and Nursing (IVDP), University Medical Centre, Hamburg, Germany
[3]Department of Occupational Medicine, Hazardous Substances and Public Health, Institution for Statutory Accident Insurance and Prevention in the Health and Welfare Services (BGW), Hamburg, Germany
Email: frank.hoffmeyer@dguv.de

How to cite this paper: Hoffmeyer, F., Beine, A., Gina, M., Zahradnik, E., Kleinmüller, O., Sander, I., Nienhaus, A. and Raulf, M. (2024) Examination of Respiratory Health-Consideration of Atopic and Non-Atopic Staff in Veterinary Practices. *Health*, **16**, 1161-1175.
https://doi.org/10.4236/health.2024.1612080

Received: October 29, 2024
Accepted: November 30, 2024
Published: December 3, 2024

Abstract

Introduction: In veterinary medicine, with its diverse exposures, employees are at increased risk of sensitization, allergies, and occupational respiratory diseases. **Methods:** In this cross-sectional study, we investigated the lung function of 103 veterinary assistants and nineteen veterinarians in veterinary practices regarding sensitization, atopy, and asthma. All participants completed a questionnaire. We determined specific IgE, and lung function using spirometry and body plethysmography according to the ATS criteria. The results were compared with the reference values of the Global Lung Initiative (GLI) based on the z-score. Subjects with known, physician-confirmed asthma or regular medication use were excluded, leaving 109 subjects. **Results:** Spirometry and body plethysmography showed repeatable results without artifacts. The median z-score of the Tiffeneau-index and the maximal mid-expiratory flow (MMEF), parameters for identifying obstructive ventilation limitations, were significantly reduced compared to the norm. Manifest obstructive airway disease was found in 6.3% (n = 2/32) atopic and 9.1% (n = 7/77) non-atopic subjects. The TLC z-score showed a normal median and normal distribution. According to the GLI reference values, 4.6% of these values were below the normal (LLN) limit. The analyses showed a relevant influence of atopy status, sensitization to furry animals, and tobacco smoking on the FEV_1/FVC ratio. No significant correlations were found between lung function and occupational characteristics. **Conclusion:** Manifest

obstructive lung disease was found in both symptom-free and symptomatic individuals. The study emphasizes the need for close monitoring of sensitized workers to detect early impairment and limit occupational effects on lung function.

Keywords

Lung Function, Occupational Medicine, Sensitization, Spirometry, Veterinary Staff

1. Introduction

Contact with laboratory animals and veterinary medicine are fields with a heightened risk of sensitization, allergy, and occupational respiratory and skin disease [1] [2]. Studies have reported that the prevalence of respiratory symptoms ranges from 40% to 60% among veterinarians [3] [4]. Most occupational lung diseases are caused by repeated, long-term exposure, with occupational asthma and chronic obstructive pulmonary disease (COPD) being the most commonly diagnosed respiratory diseases [5] [6]. Close contact with various animals and pets can lead to sensitization and allergic diseases of the upper (rhinitis) and lower respiratory tract (allergic asthma) in exposed workers [4] [7]. Occupational asthma is the leading occupational lung disease in both developing and industrialized nations, accounting for approximately 15% of all asthma cases and an annual incidence rate of up to 18 per 100,000 [8]. Based on inflammatory mechanisms, it can be categorized into allergic and non-allergic asthma [9]. Besides allergic (and infectious) risks, bacteria and fungi can cause inflammatory reactions through the inhalation of endotoxins or ß-glucans [10], leading to non-allergic reactions like non-allergic rhinitis, organic dust toxic syndrome (ODTS), non-allergic asthma, bronchitis, and COPD [11] [12].

In addition, personal characteristics such as atopy status can influence the extent of sensitization to animals, respiratory symptoms, and the impairment of lung function [13] [14]. It was found that both sensitization and exposure to laboratory animal allergens contributed independently to lung function decline in subjects who had been working with laboratory animals. Nevertheless, data for the group of veterinarians and assistant staff in veterinary practices are scarce.

Previous reports based on data from this study described determinants of exposure, work-related respiratory symptoms, and physician-confirmed diseases [4] [15]. Here, we assessed spirometry and body plethysmography in veterinarians and assistants. We investigated risk factors for lung function impairment in subjects without physician-diagnosed lung diseases and related lung function to occupational exposures and personal characteristics like atopic status and specific sensitization against cats and/or dogs.

2. Materials and Methods

2.1. Participants, Study Design, Questionnaire, and IgE Determination

These topics were discussed in detail by Hoffmeyer *et al.* [4]. Briefly, participants were recruited from veterinary practices located within a radius of up to 100 km from the Institute for Prevention and Occupational Medicine (IPA, Bochum). They filled out a questionnaire asking about the patient's history, allergic diseases, smoking habits, profession, animal contact, and current symptoms. Rhinitis and conjunctivitis were defined by symptoms of nose or eye irritation. Lower airway symptoms (coughing or wheezing, excess phlegm or sputum, and shortness of breath) were rated according to intensity (no; 0, weak; 1, mild; 2, and strong; 3) and integrated into an additive symptom score (up to 9). Measurements of specific IgE to a ubiquitous inhalation allergen mixture (screening tool; sx1), cat (e1), and dog dander (e5) were performed and values ≥ 0.35 kU/L were considered positive. Atopy status in this study was defined with an allergy screening tool (sx1).

2.2. Lung Function Measurements

Spirometry was performed using a pneumotachograph (MasterScreen®, Vyaire Medical GmbH, Höchberg, Germany) according to the ATS/ERS recommendations [16] [17]. The following parameters were assessed: Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV_1), Tiffeneau-index (Tiff., FEV_1/FVC), and maximal mid-expiratory flow (MMEF). Respective reference values for lung function parameters were chosen according to the Global Lung Function Initiative (GLI) and referring to z-scores and the lower limit of normal (LLN) [18]. Cases with FEV_1/FVC < LLN were classified as obstructive lung disease.

The residual lung volume (RV) and total lung capacity (TLC) were determined using a constant-volume whole-body plethysmograph (PWC-Body-Plethysmograph, Ganshorn, Germany). These measurements were recorded during resting breathing [19]. Cases with TLC < LLN were categorized as restrictive ventilatory failure [20]. Body plethysmographic measurements and spirometry were performed consecutively in one complete measurement cycle.

2.3. Statistical Analysis

Central tendency and dispersion were reported using either Mean/SD or Median/IQR. Appropriate tests such as the t-test, Mann-Whitney U test, or Kruskal-Wallis test were utilized for comparisons. Analysis of contingency tables was performed with either Fisher's exact test or Pearson's chi-square test. The relationship between exposure and effect characteristics was determined using Spearman's rank correlation.

The Wilcoxon Signed Rank-Test was used to compare lung function value z-scores with the theoretical median (where z-score equals 0). A p-value less than 0.05 was considered statistically significant. All statistical analyses and graphical results were performed with GraphPad Prism (version 10.1.2, GraphPad Software,

Inc., La Jolla, CA).

2.4. Ethics

The study was performed by the Declaration of Helsinki and was approved by a local Ethics Committee (Ruhr-University Bochum, registration number 17-6022).

3. Results

3.1. Subject Characteristics

We recruited 103 assistants and nineteen veterinarians. The gender distribution shows a female predominance (n = 110 vs. male n = 12). Among the 122 individuals, 13 had physician-confirmed asthma. Six participants were diagnosed with asthma after starting their careers in veterinary practice. Among them, three reported that their asthma worsened due to work, while two out of seven with preexisting asthma also experienced work-related aggravation. Out of the 13 individuals with asthma, nine were classified as atopic based on their sx1 levels. Among the remaining 109 individuals without an asthma diagnosis, 32 were atopic and 77 were non-atopic. A sensitization against furry animals (cats and/or dogs) was seen in 18 of the 41 atopic subjects analyzed (43.9%). In these atopics, the proportion of subjects with physician-confirmed asthma (n = 4/9, 44.4%) was similar to those without asthma (n = 14/32, 43.8%). One veterinarian without asthma demonstrated a slightly elevated specific IgE level to cat dander (0.44 kU/L; class 1) without being defined as atopic concerning the sx1. The use of prescription medication associated with asthma was reported by 71.4% of those with confirmed disease, while corresponding medication without an asthma diagnosis was not reported. Table 1 provides a comprehensive overview of the individual characteristics that were categorized based on asthma diagnosis (physician-based) and atopic status.

3.2. Lung Function

Spirometry was performed in all 122 subjects and a total of 433 flow-volume maneuvers and numerical absolute result sets were analyzed in detail. The within-maneuver evaluation for acceptability showed no artifacts. The examinations could be considered repeatable within a difference of 150 mL for FEV_1 in 95.9% (n = 117) and FVC in 96.7% (n = 118) of the subjects, respectively (data not shown).

Information on lung function values of workers with and without asthma, further categorized into atopic and non-atopic is shown in Table 2. In 10 workers (8.2%), a manifest obstructive ventilatory disorder was detected, with only one subject having a confirmed asthma diagnosis. In the group without known asthma, the prevalence was 6.3% (n = 2/32) in atopic and 9.1% (n = 7/77) in non-atopic subjects, respectively.

Corresponding to the results of the FVC, the subgroup of atopic asthmatics had a higher TLC z-score than expected according to GLI (IQR 0.25; 1.03; p = 0.039). Detailed data on all subgroups are shown in Table 2. There were five subjects with

Table 1. Characteristics of individuals stratified by asthma and atopy status.

		All (n = 122)	Physician-confirmed asthma (n = 13)		No history of asthma (n = 109)	
Characteristics			Atopic (n = 9)	Non-atopic (n = 4)	Atopic (n = 32)	Non-atopic (n = 77)
Age (years)	*[Med. (IQR)]*	33.0 (26.0; 45.0)	33.0 (23.5; 40.0)	41.5 (32.0; 50.3)	28.5 (24.3; 44.5)	33.0 (26.0; 45.5)
Gender						
f/m	*[n]*	110/12	7/2	4/0	27/5	72/5
Smoking habits						
never/former/current	*[n]*	71/25/26	6/2/1	3/0/1	17/7/8	45/16/16
Profession						
assistant/doctor	*[n]*	103/19	9/0	3/1	26/6	65/12
years	*[Med. (IQR)]*	7.5 (3.3; 17.5)	4.9 (3.1; 13.7)	17.2 (8.3; 27.7)	7.0 (3.2; 15.5)	8.3 (3.3; 18.1)
Practice employment						
small animals/other	*[n]*	109/13	9/0	4/0	29/3	67/10
years	*[Med. (IQR)]*	4.5 (1.8; 12.3)	2.8 (0.9; 11.4)	12.3 (3.2; 25.3)	4.6 (1.9; 9.8)	4.8 (1.9; 13.5)
Sensitization *cats +/- dogs*	*[n]*	19	4	0	14	1
Airways						
prescription drugs	*[n]*	10	7	3	0	0

Med. median, *IQR* interquartile range, Sensitization: specific IgE value ≥ 0.35 kU/L for cats and/or dogs.

Table 2. Comparison of lung function values (z-score) between individuals with and without asthma, further categorized by atopic and non-atopic status.

	Physician-confirmed asthma (n = 13)				No history of asthma (n = 109)			
	Atopic (n = 9)		Non-atopic (n = 4)		Atopic (n = 32)		Non-atopic (n = 77)	
Spirometry	z-score	p*	z-score	p*	z-score	p*	z-score	p*
FVC [Med(iQR)]	1.16 (0.22; 1.25)	0.012	0.08 (−0.35; 0.78)	0.875	0.07 (−0.59; 0.42)	0.709	0.24 (−0.40; 0.94)	0.055
FEV1	0.84 (−0.33; 1.37)	0.129	0.17 (−0.74; 0.79)	>0.999	−0.29 (−0.80; 0.12)	0.112	0.05 (−0.70; 0.58)	0.917
Tiff	−0.82 (−1.37; −0.21)	0.027	−0.23 (−0.75; 0.19)	0.500	−0.43 (−0.99; 0.20)	0.005	−0.43 (−0.88; 0.15)	<0.0001
MMEF	−0.22 (−1.03; 0.35)	0.301	0.19 (−1.00; 0.54)	>0.999	−0.39 (−1.28; 0.18)	0.009	−0.28 (−0.90; 0.42)	0.006
Bodyphethymography								
TLC	0.44 (0.25; 1.03)	0.039	−0.14 (−0.42; 0.43)	0.875	−0.06 (−0.41; 0.28)	0.403	−0.20 (−0.61; 0.52)	0.443
Obstructive lung disease Tiff z−score < −1.64	n = 1		n = 0		n = 2		n = 7	

FVC Forced Vital Capacity, *FEV*$_1$ Forced Expiratory Volume in 1 second, *Tiff* Tiffeneau-index (FEV$_1$/FVC), *MMEF* Maximum Mid-Expiratory Flow. Values are represented by z-scores, a statistical measurement that describes a value's relationship to the mean of a group of values. Z-score is measured in terms of standard deviations from the mean. *p-values indicating the statistical significance of the differences between the lung function values of the respective group and the GLI-reference (z-score = 0).

TLC z-scores below the LLN. None of these subjects with restrictive ventilation patterns had an asthma diagnosis or an additional obstructive impairment.

3.3. Risk Factors for Lung Function Impairment

The main aim of the current analysis was to identify risk factors for impaired lung function. Regular use of medication to improve lung function is a significant confounding factor for analyzing lung function impairment. These subjects and those with known respiratory disease were excluded from further analyses, leaving 109 subjects for further analyses.

a) Restrictive ventilation pattern

Five of the 109 subjects (4.6%) had TLC z-scores below the LLN, indicating restrictive impairment. All of these subjects were female assistants, three of whom were obese. The two women of normal weight were atopic and additionally sensitized against furry animals. One of them was a current smoker, and the rest were never or former smokers. All but one were working in a small animal practice.

The results regarding potential risk factors for obstructive impairment were as follows.

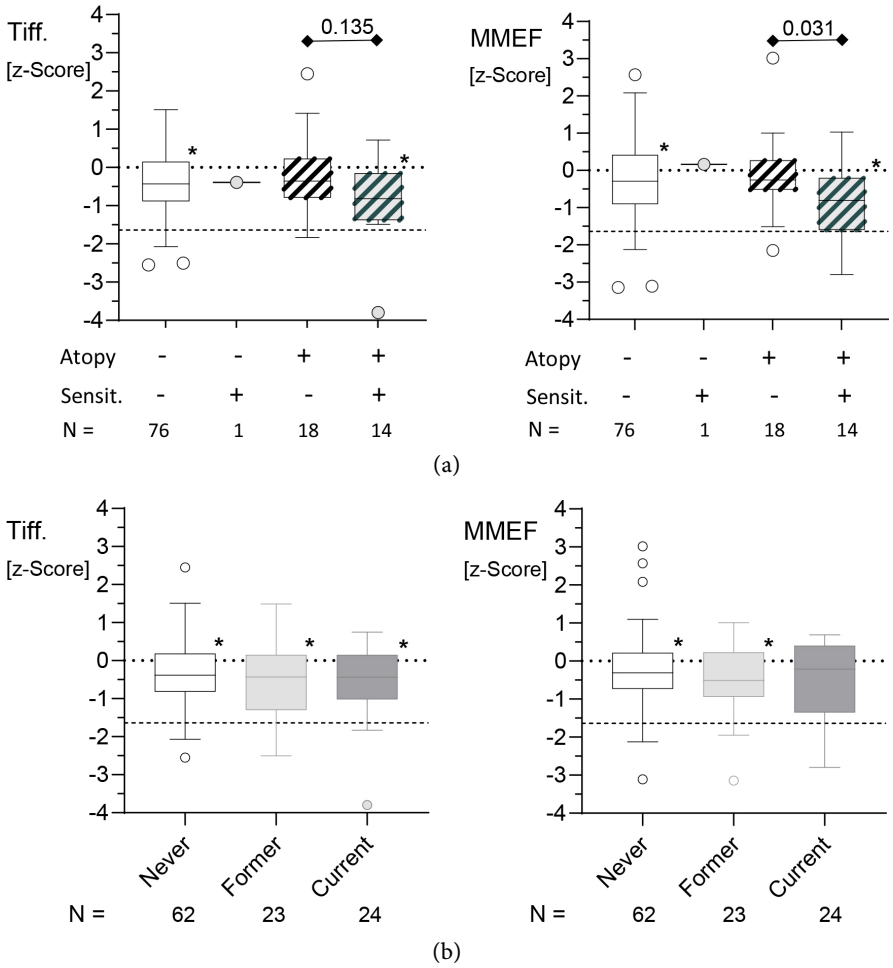
b) Obstructive ventilation pattern

Almost half of the atopic test subjects were specifically sensitized to cat and/or dog allergens.

In particular, atopic subjects with sensitization to cat and/or dog allergens showed reduced lung function parameters that indicate obstructive impairment. Significant differences in MMEF were found between atopics with specific sensitization against furry animals (−0.81 IQR −1.60; −0.20) and other atopics (−0.26 IQR −0.52; 0.28, p = 0.031). In addition, a consistent trend was observed for FEV_1 (−0.82 IQR −1.38; −0.15 vs. −0.36 IQR −0.79; 0.23, p = 0.135) (shown in **Figure 1(a)**).

The results of the MMEF and the Tiffeneau Index stratified by smoking habits are depicted in **Figure 1(b)**. Differences were found when comparing subgroups of smokers according to their underlying immunological status. Concerning current smokers, subjects with specific sensitization to furry animals had lower Tiffeneau z-scores (−0.97 (IQR −2.65; −0.31)) than non-atopic subjects without specific sensitization (−0.36 (IQR −0.65; 0.12), p = 0.091). About MMEF, the respective z-scores were significantly different (−1.50 (IQR −2.34; −0.78) vs. −0.07 (IQR −0.88; 0.48, p = 0.011)). Comparisons between never-smokers and former smokers showed no differences in the z-scores of Tiffeneau-Index and MMEF regarding atopy or specific sensitization.

Assistants and veterinarians showed a similar reduction in Tiffeneau z-score (−0.43 (IQR −0.97; 0.15) vs. −0.22 (IQR −1.00; 0.21), p = 0.510). When comparing the MMEF, assistants had lower z-values (−0.39 (IQR −0.91; 0.20 vs. −0.01 (IQR −0.52; 0.59), p = 0.067). Regarding the type of practice, no differences were found between Tiffeneau z-score for employees in mixed or large animal practices (other practices) compared to those in small animal practices (−0.71 (IQR −1.03; 0.11) vs. −0.38 (IQR −0.97; 0.18), p = 0.510). This also applied to the MMEF (−0.39 (−1.09; 0.34) vs. −0.33 (−0.88; 0.24), p = 0.704). Detailed information on the



Tiff Tiffeneau-index (FEV_1/FVC), *MMEF* Maximum Mid-Expiratory Flow; *Sensit* Sensitization, specific IgE values ≥ 0.35 kU/L for cats and/or dogs. Values are represented by z-scores, a statistical measurement that describes a value's relationship to the mean of a group of values. Z-score is measured in terms of standard deviations from the mean. *statistically significant difference compared to the lung function values of the GLI-reference.

Figure 1. Effect of immunologic status (A) and smoking habits (B) on lung function.

influence of occupation and type of practice on lung function, stratified by serologic antibody characteristics, is shown in **Table 3**. There was no significant correlation between the Tiffeneau index or the MMEF and the duration of employment, independent of atopy or sensitization against furry animals (data not shown).

3.4 Symptoms and Lung Function

Symptoms such as coughing or wheezing, phlegm or sputum, and shortness of breath were reported by 46 (42.6%) employees. All but one of the employees also suffered from rhinitis, and 44 employees stated that they only suffered from rhinitis. Subjects with lower respiratory tract symptoms had a significantly lower z-score for the Tiffeneau index (−0.65 (IQR −1.34; −0.16)) than the 19 symptom-free subjects (−0.12 (IQR −0.70; 0.21), p = 0.019). The Tiffeneau index in the

Table 3. Comparison of lung function values (z-score) of individuals with respect to occupational characteristics and categorized by immunologic conditions.

	Profession			Type of practice		
	Assistant n = 91	Veterinarian n = 17 [$]	p-value	Small animals n = 95 [$]	Others n = 13	p-value
FEV_1						
No atopy/no sensitization	n = 65 −0.43 (−0.96; 0.17)	n = 11 −0.29 (−0.84;0.14)	0.864	n = 66 −0.33 (−0.83; 0.16)	n = 10 −0.79 (−1.31; −0.20)	0.159
Atopy/No sensitization	n = 14 −0.43 (−0.79; 0.31)	n = 4 0.18 (−0.82; 0.28)	0.587	n = 16 −0.36 (−0.76; 0.28)	n = 2 −0.82, 0.15	n/a
Atopy/sensitization	n = 12 −0.82 (−1.35; −0.23)	n = 2 −1.35, 0.21	n/a	n = 13 −0.82 (−1.41; −0.24)	n = 1 0.06	n/a
MMEF						
No atopy/no sensitization	n = 65 −0.39 (−0.91; 0.33)	n = 11 −0.01 (−0.52; 0.50)	0.233	n = 66 −0.24 (−0.82; 0.42)	n = 10 −0.77 (−1.27;0.21)	0.215
Atopy/no sensitization	n = 14 −0.33 (−0.63; 0.13)	n = 4 0.51 (−0.30; 0.92)	0.122	n = 16 −0.26 (−0.54: 0.23)	n = 2 −0.39, 0.35	n/a
Atopy/sensitization	n = 12 −0.81 (−1.76; −0.33)	n = 2 −1.51, −0.14	n/a	n = 13 −0.82 (−1.68; −0.44)	n = 1 0.32	n/a

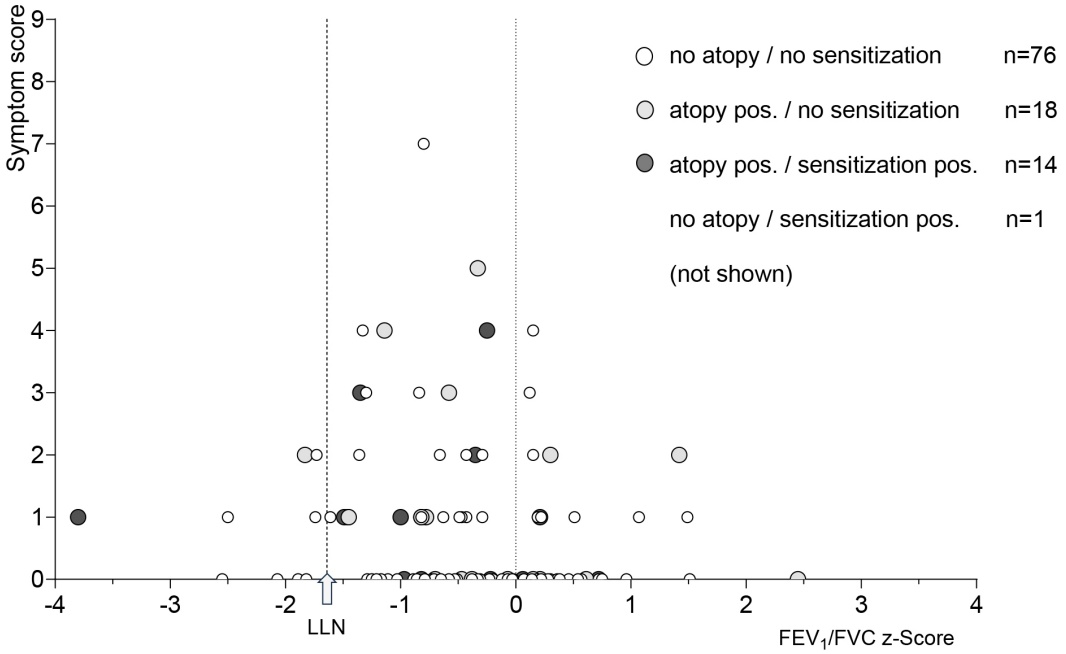
Tiff Tiffeneau-index (FEV_1/FVC), *MMEF* Maximum Mid-Expiratory Flow; *Atopy*, IgE value ≥ 0.35 kU/L for sx1. *Sensitization*, specific IgE value ≥ 0.35 kU/L for cats and/or dogs. n/a not applicable. Results are presented as median with IQR, for up to n = 3 subjects individual results are given. [$]One doctor working in a small animal practice was sensitized against cats but was not atopic.

group with only rhinitis did not differ significantly from the symptom-free subjects (p = 0.555). Similar results were obtained for the MMEF z-score in subjects with lower respiratory tract symptoms (−0.51 (IQR −1.24; 0.09)) compared to symptom-free subjects (0.16 (IQR −0.49; 0.50), p = 0.032) and for rhinitis (p = 0.171).

Nevertheless, manifest obstructive pulmonary disease (Tiffeneau z-score < −1.64) was found in 4 of 63 subjects without lower airway symptoms, which corresponds to a prevalence of 6.3%. Three of these four had rhinitis. A similar prevalence of 7.8% was found in subjects with lower airway symptoms (n = 5/46). Three of the five subjects with formal restrictive lung function patterns were symptom-free. The results for severity of lower airway respiratory symptoms and spirometry are shown in **Figure 2** (Data stratified for rhinitis are not shown).

4. Discussion

When working with animals, humans are exposed to various particulate, biological, or chemical agents [1]. These exposures can lead to specific (e.g. TH2-type) or non-specific inflammatory responses in the airways or lung parenchyma. Among the 122 individuals in our study, 13 had physician-confirmed asthma, of which 9 were atopic and 4 were non-atopic concerning sx1 level. The prevalence of 11% for physician-confirmed asthma was in the range previously reported [21] [22]. Most of the asthmatics were properly treated, and only one participant had a manifest obstructive ventilation disorder. A discussion of the prevalence of



Additive symptom score of the lower airways (up to 9); coughing or wheezing, excess phlegm or sputum, shortness of breath were rated according to intensity (0 to 3). *Tiff* Tiffeneau-index (FEV_1/FVC). Values are represented by z-scores. *LLN* lower limit of normal, the z-Score at LLN is minus 1.645. *Atopy*, IgE value ≥ 0.35 kU/L for sx1. *Sensitization*, specific IgE value ≥ 0.35 kU/L for cats and/or dogs.

Figure 2. Correlation between the severity of respiratory symptoms and spirometry.

asthma and symptoms associated with existing atopy or specific sensitization to furry animals can be found in our recent publication [4].

In our current analyses, we investigated the lung function of 109 subjects without known respiratory disease. In addition to obstructive changes, restrictive impairments were considered. Correct differentiation can be difficult if the ATS criteria for lung function tests are not met. Often the fulfillment of the acceptability and repeatability criteria is not specified [17]. In this study, we could rely on quality-assured measurements. A test result was considered indicative of disease if it fell outside the normal range. Both the ATS and ERS recommended using the 5th centile (minus 1.64 z-score) to define the lower limit of normal (LLN) for lung function parameters. Unlike percent predicted values, z-scores are free from bias due to age, height, sex, or ethnic group [18].

Typically, the diagnosis of airway obstruction is predicated on the observation of a diminished ratio of FEV_1 to FVC (Tiffeneau-Index). The degree of severity is gauged by the decrease in FEV_1, while FVC tends to remain constant. Both parameters can be assessed by spirometry. In addition, we measured the MMEF, which is sensitive to peripheral expiratory flow obstruction, and an available methodology to assess small airway function. MMEF might serve as an early indicator of obstructive pulmonary disease [23].

A restrictive disorder can be suspected from spirometry when VC is reduced and the Tiffeneau-Index either is normal or elevated. It is proven, however, only by a decrease in TLC [19]. TLC assessment is the gold standard for the diagnosis

of restrictive impairment, which is defined as TLC being below the 5th percentile of reference. In our study, the determination of TLC was based on body plethysmography in combination with quality-assured spirometry according to ATS recommendations [16]. Reference values and LLN for TLC were recently published [20].

Our subjects showed an expected TLC z-score of −0.04 and a normal distribution. Nevertheless, there were values indicating a restrictive ventilatory dysfunction concerning LLN in five subjects. Referring to the LLN of TLC corresponding to the 5th percentile, the observed prevalence of 4.6% (5 of 109) was exactly within the expected range of the GLI reference distribution [20].

In our study, the median z-scores of the Tiffeneau index and MMEF, parameters used to identify obstructive ventilatory limitation, showed a shift to the left and were significantly lower compared to the corresponding GLI data [18] [23]. Ten workers (8.2%) had a formal obstructive ventilatory disorder with a Tiffeneau z-score below the LLN. This is therefore more than the GLI reference distribution suggests [18]. The prevalence was slightly higher in non-atopic subjects (9.1% vs. 6.3% in atopic subjects). Such a prevalence in individuals who are neither atopic nor asthmatic suggests that non-allergic mechanisms should be carefully considered when investigating lung function and occupational diseases [24]. Specifically, veterinary staff are constantly exposed to animal dander during work. This dander not only contains high molecular weight allergens but also irritative components of microbial origin such as endotoxins and β-glucan. For example, pet ownership is strongly associated with high indoor endotoxin levels [25]. Additionally, veterinary staff is exposed to irritative substances like cleaning agents and disinfectants [3] [26].

Overall, subjects with respiratory symptoms had a significantly lower Tiffeneau-index z-score than symptom-free subjects, accompanied by a similar trend in MMEF z-scores. There was no association between the severity of symptoms and obstructive impairment. In addition, four symptom-free subjects had obstructive lung disease (Tiffeneau z-score < −1.64), which corresponds to a prevalence of 44.4% for obstructive individuals. This is consistent with the results in patients diagnosed with COPD. While symptoms such as chronic cough (45%), sputum production (38%), and dyspnoea on exertion (52.5%) were frequently observed, 32% reported no symptoms [27].

In subjects without asthma, no significant differences were found in the overall reduced FEV_1 and MMEF values between subjects with and without atopy. This suggests that atopy per se was not the main factor in reducing these lung function values in workers without asthma.

An important result, however, was the effect of specific sensitization. Almost half of the atopic subjects were specifically sensitized to cat and/or dog allergens. These atopic subjects with sensitization to furry animals showed reduced lung function parameters indicative of obstructive impairment. Significant differences in MMEF were found between atopics with such specific sensitization and other

atopics, suggesting that sensitization to furry animals may contribute to obstructive impairment in atopic individuals. No significant associations were found between occupation, type of practice, or duration of work and lung function parameters indicating obstructive impairment. However, exposure to animals does not only occur in an occupational context but also the personal environment [15] [21]. Eighty-two percent of the employees in our study had cats and dogs as pets. Animal allergens are also frequently found in schools and on public transport [28] [29].

Effects on respiratory health have been investigated in longitudinal studies for laboratory animal workers, but data for the veterinarians and staff group is scarce. In a 5-year follow-up study of 319 laboratory workers, an excessive decrease in FEV_1 and FVC was found in sensitized workers (FEV_1/FVC data were not provided) [30]. The decline was greatest in subjects exposed to the animals to which they were sensitized. In a study on 70 newly employed subjects a progressive lung function impairment was seen within two years from the start of exposure to laboratory animals [14]. Time-related impairment was observed in the whole study population irrespective of allergic sensitization, suggesting that exposure to animal facilities could be harmful. In a Swedish 5-year follow-up study of 88 animal-exposed laboratory technicians, no significant decrease in lung function was found [31]. The authors considered a concomitant decrease in smoking habits during the follow-up, a better working environment, and the use of anti-allergic medication as possible confounding factors.

Cigarette smoking is widely recognized as an important risk factor for diseases such as chronic bronchitis and COPD [32]. Moreover, smoking could amplify the adverse effects of occupational exposure on lung function [33]. Our results are in line with these findings and confirm the assumption of possible interactions between specific sensitization and smoking on lung function [34]. Thus, our findings underscore the importance of considering both immunological and lifestyle factors in the assessment and management of lung function. Even though smoking could explain part of the respiratory impairment, it should be emphasized that our results suggest that veterinary staff and veterinarians are potentially at risk due to their occupational exposure.

5. Limitations

Although our study provides quality-assured findings on the lung function of workers in veterinary practices, there are potential limitations that should be taken into account. This cross-sectional study recruited a total of 122 participants, including female assistants and a small number of veterinarians. Factors for non-participation could be a lack of interest in the study or concerns about disclosing animal-related symptoms to their employer. Subjects with respiratory health problems might be more willing to participate. On the other hand, people with health problems may leave work earlier, making it difficult to establish a link between health problems and exposure in the workplace (healthy worker effect) [35].

Thus, larger and longitudinal studies may provide more robust and generalizable results.

In our study, almost half of the atopic subjects were specifically sensitized to cat and/or dog allergens. Sensitization to other allergens was not analyzed. The study did not account for exposure to secondhand smoke, or irritants, which could significantly impact lung function.

6. Conclusion

The results of our study suggest that occupational exposure to furry animals and the development of sensitization against animal allergens may have a significant impact on lung function in employees. Identifying and addressing the actual workplace exposure and the early detection of workers at risk can lead to the prompt initiation of preventive measures such as workplace adjustment, regular check-ups, and guidance for quitting smoking. Objective lung function assessments possess the capability to detect alterations even when overt clinical manifestations are not present. Therefore, lung function tests (spirometry) should be used as a screening tool and preventive measure, both at an early stage and on an ongoing basis.

Acknowledgement

The authors thank the employees of the veterinary practices for their support and participation in this study.

We thank Anne Lotz and Christoph Nöllenheidt for data management.

Funding

This study (IPA-148-AllergoMed) was financially supported by Institution for Statutory Accident Insurance and Prevention in the Health and Welfare Services (BGW) and the German Social Accident Insurance (DGUV).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Lutsky, I., Baum, G.L., Teichtahl, H., Mazar, A., Aizer, F. and Bar-Sela, S. (1985) Occupational Respiratory Disease in Veterinarians. *Annals of Allergy*, 55, 153-156.

[2] Beine, A., Gina, M., Hoffmeyer, F., Lotz, A., Nöllenheidt, C., Zahradnik, E., *et al.* (2022) Skin Symptoms in Veterinary Assistant Staff and Veterinarians: A Cross-Sectional Study. *Contact Dermatitis*, **87**, 247-257. https://doi.org/10.1111/cod.14146

[3] Samadi, S., Wouters, I.M. and Heederik, D.J. (2013) A Review of Bio-Aerosol Exposures and Associated Health Effects in Veterinary Practice. *Annals of Agricultural and Environmental Medicine*, **20**, 206-221.

[4] Hoffmeyer, F., Beine, A., Lotz, A., Kleinmüller, O., Nöllenheidt, C., Zahradnik, E., *et al.* (2021) Upper and Lower Respiratory Airway Complaints among Female Veterinary Staff. *International Archives of Occupational and Environmental Health*, **95**,

665-675. https://doi.org/10.1007/s00420-021-01798-5

[5] Perlman, D.M. and Maier, L.A. (2019) Occupational Lung Disease. *Medical Clinics of North America*, **103**, 535-548. https://doi.org/10.1016/j.mcna.2018.12.012

[6] Ratanachina, J., Amaral, A.F.S., De Matteis, S., Lawin, H., Mortimer, K., Obaseki, D.O., *et al.* (2022) Association of Respiratory Symptoms and Lung Function with Occupation in the Multinational Burden of Obstructive Lung Disease (BOLD) Study. *European Respiratory Journal*, **61**, Article ID: 2200469. https://doi.org/10.1183/13993003.00469-2022

[7] Nienhaus, A., Skudlik, C. and Seidler, A. (2005) Work-related Accidents and Occupational Diseases in Veterinarians and Their Staff. *International Archives of Occupational and Environmental Health*, **78**, 230-238. https://doi.org/10.1007/s00420-004-0583-5

[8] Balmes, J., Becklake, M., Blanc, P., Henneberger, P., Kreiss, K., Mapp, C., Milton, D., Schwartz, D., Toren, K. and Viegi, G. and Environmental and Occupational Health Assembly, American Thoracic Society (2003) American Thoracic Society Statement: Occupational Contribution to the Burden of Airway Disease. *American Journal of Respiratory and Critical Care Medicine*, **167**, 787-797.

[9] Elbers, A.R.W., Blaauw, P.J., de Vries, M., van Gulick, P.J.M.M., Smithuis, O.L.M.J., Gerrits, R.P., *et al.* (1996) Veterinary Practice and Occupational Health. *Veterinary Quarterly*, **18**, 127-131. https://doi.org/10.1080/01652176.1996.9694633

[10] Rylander, R. (2010) Organic Dust Induced Pulmonary Disease—The Role of Mould Derived β-Glucan. *Annals of Agricultural and Environmental Medicine*, **17**, 9-13.

[11] Tielen, M.J.M., Elbers, A.R.W., Snijdelaar, M., van Gulick, P.J.M.M., Preller, L. and Blaauw, P.J. (1996) Prevalence of Self-Reported Respiratory Disease Symptoms among Veterinarians in the Southern Netherlands. *American Journal of Industrial Medicine*, **29**, 201-207. https://doi.org/10.1002/(sici)1097-0274(199602)29:2<201::aid-ajim11>3.0.co;2-7

[12] Guerra, S. (2005) Overlap of Asthma and Chronic Obstructive Pulmonary Disease. *Current Opinion in Internal Medicine*, **4**, 171-177. https://doi.org/10.1097/01.mcp.0000146780.33963.bf

[13] Boulay, M. and Boulet, L. (2003) The Relationships between Atopy, Rhinitis and Asthma: Pathophysiological Considerations. *Current Opinion in Allergy and Clinical Immunology*, **3**, 51-55. https://doi.org/10.1097/00130832-200302000-00009

[14] Palmberg, L., Sundblad, B., Lindberg, A., Kupczyk, M., Sahlander, K. and Larsson, K. (2015) Long Term Effect and Allergic Sensitization in Newly Employed Workers in Laboratory Animal Facilities. *Respiratory Medicine*, **109**, 1164-1173. https://doi.org/10.1016/j.rmed.2015.06.007

[15] Zahradnik, E., Sander, I., Kleinmüller, O., Lotz, A., Liebers, V., Janssen-Weets, B., *et al.* (2021) Animal Allergens, Endotoxin, and β-(1, 3)-Glucan in Small Animal Practices: Exposure Levels at Work and in Homes of Veterinary Staff. *Annals of Work Exposures and Health*, **66**, 27-40. https://doi.org/10.1093/annweh/wxab053

[16] Graham, B.L., Steenbruggen, I., Miller, M.R., Barjaktarevic, I.Z., Cooper, B.G., Hall, G.L., *et al.* (2019) Standardization of Spirometry 2019 Update. an Official American Thoracic Society and European Respiratory Society Technical Statement. *American Journal of Respiratory and Critical Care Medicine*, **200**, e70-e88. https://doi.org/10.1164/rccm.201908-1590st

[17] Berresheim, H., Beine, A., van Kampen, V., Lehnert, M., Nöllenheidt, C., Brüning, T., *et al.* (2023) ATS/ERS Spirometry Quality Criteria in Real Life. Results of Two Occupational Field Studies. *Respiratory Physiology & Neurobiology*, **315**, Article ID:

104094. https://doi.org/10.1016/j.resp.2023.104094

[18] Quanjer, P.H., Stanojevic, S., Cole, T.J., Baur, X., Hall, G.L., Culver, B.H., *et al.* (2012) Multi-Ethnic Reference Values for Spirometry for the 3-95-Yr Age Range: The Global Lung Function 2012 Equations. *European Respiratory Journal*, **40**, 1324-1343. https://doi.org/10.1183/09031936.00080312

[19] Criée, C.P., Sorichter, S., Smith, H.J., Kardos, P., Merget, R., Heise, D., *et al.* (2011) Body Plethysmography—Its Principles and Clinical Use. *Respiratory Medicine*, **105**, 959-971. https://doi.org/10.1016/j.rmed.2011.02.006

[20] Hall, G.L., Filipow, N., Ruppel, G., Okitika, T., Thompson, B., Kirkby, J., *et al.* (2021) Official ERS Technical Standard: Global Lung Function Initiative Reference Values for Static Lung Volumes in Individuals of European Ancestry. *European Respiratory Journal*, **57**, Article Id: 2000289. https://doi.org/10.1183/13993003.00289-2020

[21] Samadi, S., Spithoven, J., Jamshidifard, A., Berends, B.R., Lipman, L., Heederik, D.J.J., *et al.* (2011) Allergy among Veterinary Medicine Students in the Netherlands. *Occupational and Environmental Medicine*, **69**, 48-55. https://doi.org/10.1136/oem.2010.064089

[22] Langen, U., Schmitz, R. and Steppuhn, H. (2013) Häufigkeit allergischer Erkrankungen in Deutschland. *Bundesgesundheitsblatt—Gesundheitsforschung—Gesundheitsschutz*, **56**, 698-706. https://doi.org/10.1007/s00103-012-1652-7

[23] Knox-Brown, B., Mulhern, O. and Amaral, A.F.S. (2021) Spirometry Parameters Used to Define Small Airways Obstruction in Population-Based Studies: Systematic Review Protocol. *BMJ Open*, **11**, e052931. https://doi.org/10.1136/bmjopen-2021-052931

[24] Iversen, M. and Pedersen, B. (1990) Relation between Respiratory Symptoms, Type of Farming, and Lung Function Disorders in Farmers. *Thorax*, **45**, 919-923. https://doi.org/10.1136/thx.45.12.919

[25] Heinrich, J., Gehring, U., Douwes, J., Koch, A., Fahlbusch, B., Bischof, W., *et al.* (2001) Pets and Vermin Are Associated with High Endotoxin Levels in House Dust. *Clinical & Experimental Allergy*, **31**, 1839-1845. https://doi.org/10.1046/j.1365-2222.2001.01220.x

[26] Samadi, S., van Eerdenburg, F.J.C.M., Jamshidifard, A., Otten, G.P., Droppert, M., Heederik, D.J.J., *et al.* (2012) The Influence of Bedding Materials on Bio-Aerosol Exposure in Dairy Barns. *Journal of Exposure Science & Environmental Epidemiology*, **22**, 361-368. https://doi.org/10.1038/jes.2012.25

[27] Bednarek, M., Maciejewski, J., Wozniak, M., Kuca, P. and Zielinski, J. (2008) Prevalence, Severity and Underdiagnosis of COPD in the Primary Care Setting. *Thorax*, **63**, 402-407. https://doi.org/10.1136/thx.2007.085456

[28] Dotterud, L.K., Van, T.D., Kvammen, B., Dybendal, T., Elsayed, S. and Falk, E.S. (1997) Allergen Content in Dust from Homes and Schools in Northern Norway in Relation to Sensitization and Allergy Symptoms in Schoolchildren. *Clinical & Experimental Allergy*, **27**, 252-261. https://doi.org/10.1111/j.1365-2222.1997.tb00703.x

[29] Zahradnik, E. and Raulf, M. (2017) Respiratory Allergens from Furred Mammals: Environmental and Occupational Exposure. *Veterinary Sciences*, **4**, Article 38. https://doi.org/10.3390/vetsci4030038

[30] Portengen, L., Hollander, A., Doekes, G., de Meer, G. and Heederik, D. (2003) Lung Function Decline in Laboratory Animal Workers: The Role of Sensitisation and Exposure. *Occupational and Environmental Medicine*, **60**, 870-875. https://doi.org/10.1136/oem.60.11.870

[31] Sjöstedt, L., Willers, S. and Ørbæk, P. (1993) A Follow-up Study of Laboratory Animal Exposed Workers: The Influence of Atopy for the Development of Occupational Asthma. *American Journal of Industrial Medicine*, **24**, 459-469. https://doi.org/10.1002/ajim.4700240410

[32] Lugade, A.A., Bogner, P.N., Thatcher, T.H., Sime, P.J., Phipps, R.P. and Thanavala, Y. (2014) Cigarette Smoke Exposure Exacerbates Lung Inflammation and Compromises Immunity to Bacterial Infection. *The Journal of Immunology*, **192**, 5226-5235. https://doi.org/10.4049/jimmunol.1302584

[33] Blanc, P.D. and Torén, K. (2007) Occupation in Chronic Obstructive Pulmonary Disease and Chronic Bronchitis: An Update. *The International Journal of Tuberculosis and Lung Disease*, **11**, 251-257.

[34] Tommola, M., Ilmarinen, P., Tuomisto, L.E., Haanpää, J., Kankaanranta, T., Niemelä, O., *et al.* (2016) The Effect of Smoking on Lung Function: A Clinical Study of Adult-Onset Asthma. *European Respiratory Journal*, **48**, 1298-1306. https://doi.org/10.1183/13993003.00850-2016

[35] Stayner, L., Steenland, K., Dosemeci, M. and Hertz-Picciotto, I. (2003) Attenuation of Exposure-Response Curves in Occupational Cohort Studies at High Exposure Levels. *Scandinavian Journal of Work, Environment & Health*, **29**, 317-324. https://doi.org/10.5271/sjweh.737