OCCUPATIONAL RESPIRATORY DISEASE IN EASTERN SLOVAKIA BETWEEN 1990–2021: A SHIFT FROM AGRICULTURE TO INDUSTRIAL MANUFACTURING

Ľubomír Legáth[1], Ivan Tkáč[2], Petra Dittrichová[1], Ivan Perečinský[3], Miroslava Matejová[1], Slavomír Perečinský[1]

[1]Department of Occupational Medicine and Clinical Toxicology, Medical Faculty, Pavol Jozef Šafárik University and L. Pasteur University Hospital, Košice, Slovak Republic

[2]Department of Internal Medicine 4, Medical Faculty, Pavol Jozef Šafárik University and L. Pasteur University Hospital, Košice, Slovak Republic

[3]Department of Urology, University Hospital J. A. Reiman, Prešov, Slovak Republic

SUMMARY

Objectives: Occupational allergic respiratory diseases frequently occur in individuals working in the agricultural and food production sectors, textile manufacturing, and industries involving exposure to isocyanates. The study aimed to describe trends surrounding the prevalence of occupational asthma (OA), occupational rhinitis (OR), and occupational hypersensitivity pneumonitis (OHP) in Eastern Slovakia between 1990–2021.

Methods: All cases of OA, OR, and OHP registered in a database at the Louis Pasteur University Hospital in Košice, Slovakia, between 1990 and 2021, were divided into categories based on economic sector (agricultural, food production sectors, textile manufacturing, healthcare, industrial manufacturing, and tertiary sector) and causal agent. Changes in disease prevalence, causal agents, and economic sector association over time were analysed.

Results: There were 287 occupational respiratory cases (179 OA, 65 OR, and 43 OHP cases). The annual prevalence of OA declined significantly over the study period ($p < 0.05$). Overall, there was a significant decrease in cases from the agricultural ($p < 0.001$) and an increase in the industrial manufacturing ($p < 0.01$). The number of cases due to farming agents fell markedly over the study period, while metalworking fluids (MWFs) were found to be the most common causes of allergic respiratory diseases since 2018.

Conclusions: This study found a decrease in the number of OA cases, as well as changes in economic sectors and causal agents associated with OA and OHP, specifically, in the agricultural sector, with MWFs from the industrial manufacturing sector now being the most common aetiological agent.

Key words: agriculture, causal agents, metal working fluids, occupational asthma, occupational hypersensitivity pneumonitis, occupational rhinitis

Address for correspondence: S. Perečinský, Department of Occupational Medicine and Clinical Toxicology, Medical Faculty, Pavol Jozef Šafárik University and L. Pasteur University Hospital, Rastislavova 43, 04190 Košice, Slovak Republic. E-mail: slavomir.perecinsky@upjs.sk

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INTRODUCTION

Allergic respiratory diseases are common occupational ailments. The most frequent conditions are occupational asthma (OA), occupational rhinitis (OR), and occupational hypersensitivity pneumonitis (OHP). All of the aforementioned had traditionally a high prevalence in agricultural and food production sectors, textile manufacturing, wood industry, and work that involves isocyanates exposure. However, several European countries have recently experienced changes in the patterns of causative agents and economic sectors associated with these diseases, along with a concomitant increase in their prevalence. Several datasets from Europe suggest a declining trend of OA due to high molecular weight (HMW) antigens, isocyanates, and aldehydes (1). In contrast, cleaning product-related OA cases induced by chloramine and quaternary amines have increased (2, 3). Furthermore, in the UK, there was an observed decreasing trend of OHP in agriculture but a dramatic rise in cases associated with metalworking fluids (MWFs) (4).

Most of the studies that have investigated trends in occupational allergic respiratory diseases have only analysed OA; thus, there is limited data concerning OR and OHP. Furthermore, the majority of these studies have been performed in Western (5–8) or Northern Europe (9, 10). Less data come from the Central European region, including the Slovak Republic. Countries in this region are post-communist countries with different economic mechanisms that subsequently joined the European Union in 2004. Therefore, the changes in occupational respiratory diseases in these countries are not necessarily comparable to Western European countries. In our previous study, we analysed cases of OA from 1980 to 2016 in a part of Eastern Slovakia. We found a decrease in cases in agriculture and an increase in cases due to low molecular weight (LMW) agents (11). That study, however, did not concern OR and OHP. In the present study, we aimed to describe specific trends in the prevalence of OA, OR, and OHP in Eastern Slovakia from 1990 to 2021. The second aim was to assess the changes in these diseases according to economic sectors and aetiological agents. Considering the results of our previous study (12), we focused in more detail on the agricultural sector.

MATERIALS AND METHODS

Data Collection

All cases of occupational diseases in Eastern Slovakia are registered in a database overseen by the Department of Occupational Medicine and Clinical Toxicology, University Hospital, Košice. The department is a tertiary referral centre for two Eastern Slovakian regions (Košice and Prešov). In the Slovak Republic, occupational diseases include not only allergic OA and OR but also irritant subtypes of disorders. Both reactive airway and reactive upper airway dysfunction syndromes (RADS/RUDS), and low dose RADS/RUDS ("not-so-sudden irritant asthma/rhinitis") are recognized as occupational diseases. In the Slovak Republic, the regulation stipulates that if a patient suffers from both asthma and rhinitis caused by the same aetiological agent, only OA is recognized as an occupational disease. This study included all cases of OA, OR, and OHP registered in our Department between 1990 and 2021.

Diagnostic Procedures

If the patient exhibits symptoms of OA, patients undergo physical examination and basic lung function tests. Then, patients are always examined by an allergologist where the skin prick tests or serum-specific IgE antibodies tests are realized. First diagnostic method used here is the elimination/re-exposure test. The results of the elimination/re-exposure test are considered positive if the clinical symptoms are absent while the patient is out of the workplace, and a worsened clinical state is observed after the repeated exposition. Secondly, a specific inhalation challenge (SIC) is performed by inhalation of the suspected allergy-inducing agent from the workplace. The last diagnostic method is the serial bronchoprovocation test (BPT), consisting of repeated methacholine BPT. The first methacholine BPT is performed while the patient is exposed to asthma-inducing agents in the workplace. Then the second methacholine BPT is performed, after the patient is excluded from the workplace, usually during his work disability. The severity of bronchial hyperresponsiveness (BHR) after each test is compared. The serial BPT is positive if the BHR is milder or not present during the work absence compared to the results of the first test. The positivity of any methods mentioned above, and positive hygienic monitoring confirm OA (11). In contrast to some other countries, in Slovakia, the realisation of SIC is not mandatory for recognition of OA. Similarly, after suspicion of OR, patient(s) should undergo an ear, nose and throat examination and should be examined by an allergologist. The key diagnostic method is the specific nasal provocation test (NPT), which was introduced in our Department in 2003. At present, most patients undergo specific NPTs, although, in some cases, rhinitis could be recognised as an occupational disease on the base of positive skin tests or serum-specific IgE antibodies only. It is more difficult to identify whether low dose RADS/RUDS is recognized as occupational OA or OR. It is usually recognized after the exclusion of the allergic origin of symptoms and a clear association of symptoms with the associated workplace. If circumstances allow, objective methods are always used – elimination/re-exposure tests, serial peak expiratory flow monitoring, serial BPT, or simulation of working conditions with simultaneous monitoring of spirometry or rhinomanometry (typically cleaning and disinfection solutions). Diagnosis of OHP was based on an algorithm which we described in our previous study (12). Patients underwent lung-function tests, where vital capacity (VC), total lung capacity (TLC), forced expiratory volume in one second (FEV1), and pulmonary diffusing capacity – gas transfer for carbon monoxide (TLCO) decreased after exposure to antigen. Analysis of bronchoalveolar fluid was also conducted, revealing the presence of typical lymphocytosis. In all patients, chest X-rays and high-resolution computed tomography (HRCT) scans were conducted. An interstitial, reticulonodular pattern was considered a typical X-ray for HP. An HRCT scan was considered typical for HP if it displayed ground-glass opacities and/or centrilobular nodularity. In the fibrotic form of HP, lung fibrosis, including honeycombing, was present. To make a differential diagnosis for other interstitial processes, surgical lung biopsies were needed in some patients. An improvement in lung function after cessation of exposure was helpful in the differential diagnosis process. Searching for the aetiological agent was based on the positivity of precipitin tests. In patients with suspected MWFs induced HP, the samples of MWFs were analysed for bacteria and fungi using the specific culture media. Antigen extracts were produced from the microorganisms isolated from the MWFs. The antigens were prepared based on the characteristics of individual strains according to the valid procedures of the Department of Clinical Microbiology, National Institute of TB, Respiratory Diseases and Thoracic Surgery, Vyšné Hágy (12). In other types of OHP (e. g., farmer's lung), specific IgGs with commercially available kits were evaluated. Specific inhalation challenge in the diagnostic algorithm of OHP is not utilised as standard in our Department.

Statistical Analysis

Using the patient database from our Department, we retrospectively collected data concerning the age at which an occupational disease was reported, the sex and economic sector in which the patient worked, and causal agents. Occupational disease prevalence in the years 1990–2021 was compared among successive four 8-year periods. Similarly, patient's age for OA, OR, and OHP was compared among successive four 8-year periods. Economic sectors were divided into six categories, including agriculture, food production, textile manufacturing, health care, several types of industry manufacturing, and tertiary sector. Aetiological agents were divided into eight categories: agricultural agents, flour, textile agents, cleaning products, LMW agents except for cleaning products, MWFs, microorganisms (excluding bacteria and moulds in MWFs), and other agents (wood and cold). Aetiological-agent categories were grouped into eight 4-year periods that spanned the entire 32-year study period. Statistical analyses were conducted using the software SigmaStat Version 3.5 (Systat Software, San Jose, CA, USA). Data are displayed as arithmetic mean ± standard deviation (SD), median (25%–75%) or as percentages. If the data did not reflect normal distribution, non-parametric tests were used. For comparisons among the groups, analysis of variance

(ANOVA) with post-hoc Tukey test, or Kruskal-Wallis ANOVA with post-hoc Dunn test were used where appropriate. The study was approved by the Ethics Committee in Louis Pasteur University Hospital, Košice (2022/EK/04025).

RESULTS

Between 1990 and 2021, there were 287 cases of OA, OR, and OHP reported in Eastern Slovakia. Comparison of 8-year periods was statistically significant ($p=0.008$) with the highest average in the number of cases in the years 1990–1997 (12.8 ± 5.9 per year) and the lowest in the years 2006–2013 (5.1 ± 4.0). The most common disease was OA, with peak prevalence occurring in the years 1990–1997, and a further decline in cases in the next three 8-year periods ($p_{ANOVA} = 0.009$) with comparisons between the first period next three periods being significant by post-hoc test ($p<0.05$). The annual number of OR cases remained stable throughout the study period. There was a non-significant slightly upward trend in OHP cases due to an MWF-induced outbreak between 2017 and 2021 (Table 1).

Women were more frequently affected by OA, OR, and OHP during most of the study period (Table 2). Patients with OR were significantly younger compared to those with OA and OHP (median age 38 years vs. 48 years and 49 years, respectively, $p<0.001$). Overall, during the study period, the age showed a significantly increasing trend ($p_{ANOVA} = 0.002$). For OR, the trend was statistically significant ($p_{ANOVA} < 0.001$), while for OA and OHP, this trend was not statistically significant.

Table 1. Numbers of occupational asthma, occupational rhinitis, and occupational hypersensitivity pneumonitis cases and trends in Eastern Slovakia (1990–2021)

Time period	Number of cases		
	Occupational asthma	Occupational rhinitis	Occupational hypersensitivity pneumonitis
	179	65	43
1990–1993	44	11	5
1994–1997	34	7	1
1998–2001	16	6	5
2002–2005	25	6	2
2006–2009	8	4	0
2010–2013	15	13	1
2014–2017	21	13	0
2018–2021	16	5	29

***Table 2.** Proportion of females and males during each period*

Time period	Females/males (number of cases)		
	Occupational asthma	Occupational rhinitis	Occupational hypersensitivity pneumonitis
1990–1993	40/4	10/1	2/1[#]
1994–1997	23/11	5/2	1/0
1998–2001	9/7	4/2	3/2
2002–2005	7/8	4/2	1/1
2006–2009	5/3	3/1	0/0
2010–2013	10/5	11/2	0/1
2014–2017	12/9	9/4	0/0
2014–2017	6/10	3/2	7/21

[#]missing data in 2 patients

In terms of economic sectors, OA most frequently occurred in the agricultural sector, while OR was common in food production and rare in agriculture. Until 2018, OHP was most frequently recognized in the agriculture sector. However, since 2019, cases have been found exclusively in industrial manufacturing as machine operator's lung (Table 3).

Overall, there was a marked downward trend in cases from the agricultural sector during the entire study period ($p_{ANOVA} = 0.00003$). This drop in cases was observed after the first period in which the mean number of cases was 6.1±4.1 per year. The post-hoc comparison between the period 1990–1997 and the next three periods was highly significant ($p<0.001$). In contrast, reported cases in the industrial sector increased significantly ($p_{ANOVA}<0.01$). The increase was observed mainly in the last period (2014–2021). The average number of patients with industry-associated occupational diseases in this period was 5.3±4.9 per year which was significantly higher when compared with both the first and the second period ($p=0.017$) (Fig. 1).

Between 1990 and 1997, agricultural agents were generally the most common cause of occupational respiratory diseases. However, there was a dramatic downward trend in cases after

***Table 3.** Numbers of occupational asthma, occupational rhinitis, and occupational hypersensitivity pneumonitis cases according to economic sector in Eastern Slovakia (1990–2021)*

Economic sector	Occupational asthma n (%)	Occupational rhinitis n (%)	Occupational hypersensitivity pneumonitis n (%)
Agriculture	56 (31)	4 (6)	12 (28)
Food production	48 (27)	30 (46)	1 (2)
Textile manufacturing	20 (11)	12 (18)	0 (0)
Health care	13 (7)	8 (12)	0 (0)
Industrial manufacturing	34 (19)	8 (12)	28 (65)
Tertiary sector	7 (4)	3 (5)	2 (5)
Military	1 (1)	0 (0)	0 (0)

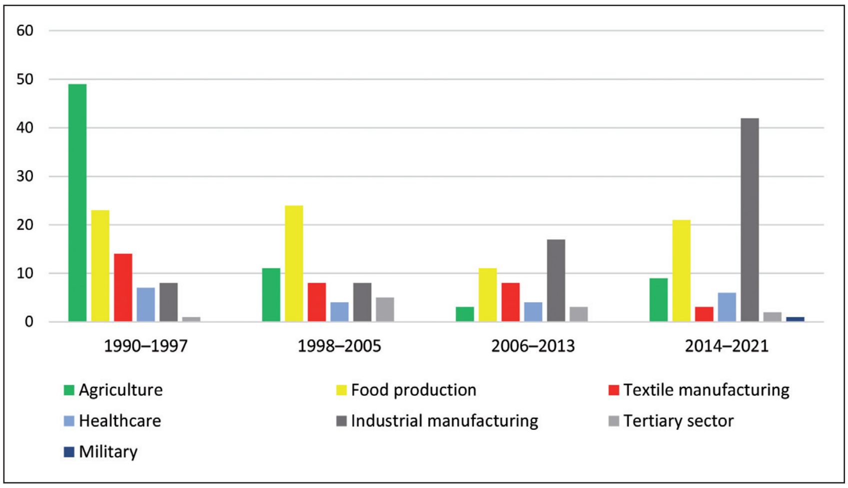

Fig. 1. *Occupational asthma, occupational rhinitis, and occupational hypersensitivity pneumonitis prevalence in the years 1990–2021 among successive four 8-year periods according to economic sectors in Eastern Slovakia.*

1997. From agricultural agents, the most prominent were cow allergens, although plant's allergens were common too. These agents induced especially OA. In the agriculture sector, microorganisms were exclusively causal agents for OHP and not for OA and OR. Pesticides were not identified as disease agents. Consequently, flour was the dominant causal agent during most periods. In contrast, starting in 2010, there was an increase in cases due to LMW agents and MWFs exposure, where MFWs exhibited a significantly increasing trend. During the period between 2018 and 2021, MWFs accounted for 57% of all reported occupational respiratory disease cases (Fig. 2).

The most common LMW agents were isocyanates (12%) and isopropyl alcohol (12%). Isopropyl alcohol was the cause of low dose RUDS. Other agents were heterogeneous, usually occurring in one or two patients only. In one case, RADS was reported in a patient after a sudden exposure to a large amount of nitrogen oxide. One case of RUDS was reported after massive exposure to chlorine gas. The proportion of cases due to cleaning agents was nearly the same during the study period, peaking between 2014 and 2017. Chlorine-based cleaning agents were the most common products that induced respiratory diseases (7 out of 18 patients). In 5 patients with exposure to multiple cleaning products, the exact agent was undetermined. All casual agents are shown in Table 4.

Table 4. *List of casual agents inducing occupational asthma, occupational rhinitis, and occupational hypersensitivity pneumonitis in Eastern Slovakia (1990–2021)*

Agens	n
Plants	39
Animals	44
Flour and grain	77
Textile (wool, cotton, synthetics, latex, rubber)	30
Low molecular weight agents (isocyanates, chloride, aldehydes, acrylates, metals, glues, resins, plastics, solvents, oxides and hydroxides)	48
Microorganisms (bacteria, moulds, mites)	18
Metal working fluids	31
Others	
Wood dust	4
Cold	1

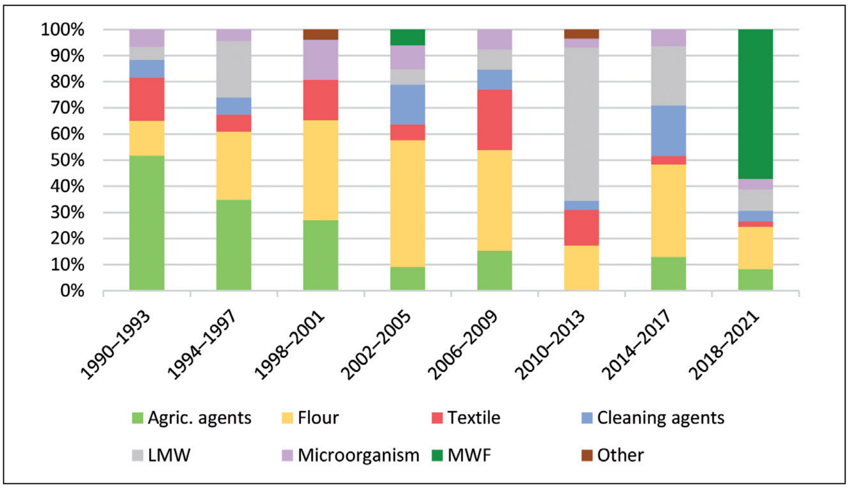

Fig. 2. *Proportion of different causal agents according to 4-year time periods.*

Agric. – agricultural; LMW – low molecular weight agents; MWFs – metal working fluids

DISCUSSION

This study found a marked decline in OA cases and a relatively stable trend in reported cases of OR and OHP. In terms of aetiological agents, cases attributed to agricultural work and textile manufacturing exposure significantly declined over the study period. Conversely, cases due to LMW agents and MWFs in industrial manufacturing increased.

We performed a long-term analysis that investigated important changes in the epidemiology of occupational respiratory diseases according to the economic sectors in the Slovak Republic. We found that the average annual proportion (during 1990–2021) of OA, OR, and OHP in Eastern Slovakia was 4.07% of all occupational diseases which is in correlation with data from all Slovakia (4.50%) (data obtained from the National Health Information Centre).

Most of the reported cases in the early 1990s resulted from exposures that occurred during the socialist economy. Previous studies from the Central European region were primarily concerned with isolated instances of specific occupational diseases, and thus, OA, OR, and OHP were not analysed together. An older study from the Czech Republic confirmed that between 1992 and 2005 OHP occurred sporadically, with the most frequent type being farmer's lung (13). In Poland and Hungary, the number of recognized OA cases has declined since 2000, with flour being the most common causal agent (14, 15). A Polish study showed that OA was the second most common occupational disease in farmers, accounting for 12% of cases, OR and OHP occurred in about 5% of cases (16). In our study, OA typically occurred in the agricultural sector; however, the trend over time was significantly negative. In a previous study from Iceland, the authors suggested that decreases in agricultural OA cases could have been due to improvements in farming conditions (9). However, a more recent review has confirmed that livestock farmers' airborne exposure to organic dust has not substantially changed over the last 30 years and currently remains high (17). In Poland and Finland, there was a marked fall in OA within the agriculture sector due to the decrease in cattle when these countries joined the European Union (18, 19). In Slovakia, there was a decrease in cattle quantity by two-thirds in 2008 compared to 1990 and this decreasing trend continues (20). It was also found that there was a change in the volume of plant and animal production. There was an increase in plant production (€670.95 million in 2000 compared to €1,238.20 million in 2019) and a decrease in animal production (€1,077.84 million in 2000 compared to €765.66 million in 2019) (21). In 1989, more than 360,000 individuals were employed within the agriculture sector (20), this number had fallen to approximately 72,000 by 2019 (20). Similarly, in the UK farming is currently not a common cause of OHP; cases of MWF-induced OHP, however, are on the rise (4). This result was also found in our study, where "farmer's lung" was replaced by "machine operator lung".

Our study has some limitations. First, despite the long-term study period, the interpretation of results could be hampered by the relatively small number of cases in each disease group and mainly descriptive statistic methods used. Secondly, we were unable to analyse each industrial manufacturing sector and type of LMW agents separately, due to the heterogeneity of the agents. Only the isocyanates and isopropyl alcohol occurred with frequency. Third, even though we were able to confirm the increasing importance of MWFs (especially for OHP) in 2017–2021, all reported cases occurred during a single outbreak (12). In general, most outbreaks occurred in the automotive industry (22), which is dominant in the Western regions of the Slovak Republic rather than in the Eastern ones. Although no outbreaks were reported from Western Slovakia, it is possible that more cases of OHP could be detected in that region. Then, due to the COVID-19 pandemic, fewer patients were admitted to our Department in the years 2020 and 2021. Thus, it is probable, that some patients, especially those with OR and OA, were overlooked during the pandemic. This is supported by the fact that no cases of OR were reported in 2021. Furthermore, it was confirmed, that due to time pressures and work overload for general practitioners, identifying OA was a low priority for primary healthcare workers (23). A potential bias exists for low dose RADS/RUDS cases because, since 2000, we have utilized a wider spectrum of objective methods compared to the 1990s. However, despite this fact, we do not expect this to impact cases within the agriculture and textile manufacturing sectors because most OA cases in these areas are still recognized on the base of skin tests or specific IgE antibodies. Interestingly, OR was rarely recognized in the agriculture sector, which is in concordance with a study performed on the Costa Rica population (24). However, we cannot exclude the occurrence of OA as once it is recognized, rhinitis then is not registered in the database of Departments.

The results of our study indicate that there is a need to actively search for other aetiological factors in the agriculture sector because we found only cases induced by typical allergens such as cows, pollen, and microbes. However, workers in agriculture are at risk of exposure, particularly to pesticides, livestock production facilities, agricultural dust, and biomass and crop burning (25). Additionally, with the changing increase in plant production and decrease in animal production, OR will probably occur more frequently compared to the past. In our previous study, we confirmed that BHR was induced more frequently by animal and mould allergens, whereas pollen rather induces allergic rhinitis without BHR (26).

The prevention of occupational respiratory diseases is difficult, especially for MWFs occupational hypersensitivity pneumonitis. It is practically impossible to perform complete decontamination of MWFs. Changing fluids and cleaning pipes has only a short-term effect. The risk of diseases can be reduced by changing technological processes. First, it is necessary to develop a technology that eliminates the need for recirculation of MWFs. In the case of some alloys, it is also possible to use dry processing (22). As part of secondary prevention, regular monitoring of workers and cooperation of practical physicians, pulmonologists and specialized occupational medicine workplaces are important. A fundamental step for the successful management and prognosis of the patient is the early removal of the worker from the exposure.

CONCLUSIONS

We found that, over the last 32 years, there have been marked changes in the prevalence of occupational asthma, the economic sectors in which it occurs, and the causal agents behind occupational asthma and occupational hypersensitivity pneumonitis. Specifically, there has been a significantly negative trend in the number of cases in the agricultural sector, with metalworking fluids from the industrial manufacturing sector now being the most common aetiological agent.

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Conflicts of Interest

None declared

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