Association between exposure to external airborne agents and autoimmune disease

Seunghyun Lee [a,1], Xiaoxue Ma [b,1], Wanhyung Lee [c,*]

[a] Department of Occupational and Environmental Medicine, College of Medicine, Gachon University, Incheon, Republic of Korea
[b] Department of Pediatrics, The First Hospital of China Medical University, Shenyang, China
[c] Department of Preventive Medicine, College of Medicine, Chung-Ang University, Seoul, Republic of Korea

ARTICLE INFO

ABSTRACT

The etiology of autoimmune disease pathogeneses remains obscure, and the impact of general environmental or occupational exposure to external airborne agents (EAA) on autoimmune diseases remains understudied. This study was conducted to elucidate the association between exposure to EAA and the risk of autoimmune diseases according to exposure type. From the NHIS-NSC (2002–2019), 17,984,963 person-years were included in the data analysis. Autoimmune diseases were categorized based on the InterLymph classification. We estimated the incidence and rate ratio of autoimmune diseases according to the EAA exposure. Association between exposure and autoimmune diseases was investigated using logistic regression analysis, adjusted for potential confounders. Of the 1,082,879 participants, 86,376 (8.0%) were diagnosed with autoimmune diseases. Among these, 208 (14.1%) experienced severe exposure to EAA. Total EAA exposure was significantly associated with any autoimmune disease (OR: 1.29, 95% CI: 1.11–1.49) and organ-specific diseases (OR: 1.28, 95% CI: 1.08–1.53). Inorganic dust exposure was associated with organ-specific diseases (OR, 1.38; 95% CI: 1.01–1.81). Exposure to other dust was significantly associated with any autoimmune disease (OR: 1.35, 95% CI: 1.10–1.66), connective tissue diseases (OR: 1.43, 95% CI: 1.03–1.99), and organ-specific diseases (OR: 1.28, 95% CI: 1.00–1.65). Exposure to EAA was predominantly related to psoriasis, rheumatoid arthritis (RA), and type 1 diabetes (T1DM). We found that exposure to EAA is a potential risk factor for autoimmune diseases, especially psoriasis, RA, and T1DM. Our findings provide insight into the role of exposure to severe airborne agents in the pathogenesis of autoimmune diseases.

1. Introduction

Autoimmune diseases are a complicated set of chronic diseases in which the deficiency of autoimmune tolerance and the imbalance and abnormal activation of innate and adaptive immunity play an important role. In terms of the mechanism of injury, the immune system cannot distinguish between autoantigens and foreign antigens, resulting in an immune response attack and inflammatory damage to its own organs and tissues (Conrad et al., 2022).

Autoimmune diseases can be divided into organ-specific diseases and connective tissue diseases. In organ-specific diseases, the immune system only attacks one or more specific organs in the body, usually involving the response to the antigen expressed only in that organ, such

as type 1 diabetes, Graves' disease, and multiple sclerosis. In connective tissue diseases, including systemic lupus erythematosus, no particular cell type is targeted and the response is directed against antigens that are widely expressed throughout the host. Nevertheless, the recognition of widely expressed specific antigens can lead to organ selectivity, such as in rheumatoid arthritis (RA) (Marrack et al., 2001).

Although autoimmune diseases are considered rare, their incidence has increased by approximately 9% over the past three decades (Lerner et al., 2015). The prevalence of autoimmune diseases is 3–5% in the general population, predominantly affecting women. A recent study reported that the mortality rate of autoimmune diseases as the underlying cause was estimated to be approximately 15 per million people (Mitratza et al., 2021). In 2023, the global annual medical expenditure

for autoimmune disorders expected increase by \$149 billion (Puustinen et al., 2020).

Although the understanding of the complex etiologies and autoimmune disease pathogeneses remain obscure, some non-modifiable characteristics are generally accepted as possible risk-elevating factors for autoimmune diseases. These include genetic susceptibility and lifestyle factors such as sex, tobacco use, nutrition, drugs, and infections (Barragán-Martínez et al., 2012). Relatively few studies have reported the role of external airborne agents (EAA) exposure in the general or occupational environment in triggering autoimmune disease development or progression (Celen et al., 2022; da Silveira Fleck et al., 2021; Moroni et al., 2012). EAA, such as airborne dust, inorganic dust, organic dust, chemical compounds, vapor, and fumes, exist in all places, and most people are unaware of them through their environment and daily lifestyle. Therefore, it is impossible for humans to avoid exposure to EAA, which constitutes a health hazard.

Given that EAA can enter the human body via inhalation, previous studies have focused on the association between EAA exposure and the respiratory system (Parks et al., 1999; Rabbani et al., 2023; Chen et al., 2022). EAA are recognized by circulating cells as damage-associated molecular patterns, and multimeric protein scaffolds called inflammasomes are formed, which can induce an autoinflammatory reaction (Torén et al., 2022). The inflammatory reaction has a cascade effect, leading to the activation of pro-caspase-1 by proteolytic cleavage and the conversion of pro-interleukin(IL)− 1β and pro-IL-18 to the bioactive form, which is released into the bloodstream. IL-1β is one of the main effector molecules that drives autoinflammatory processes and acts on the effector cells of the adaptive immune system. A large number of inflammatory mediators released by chronic inflammation act as autoantigens and trigger autoimmune diseases (Bengalli et al., 2013).

To date, most studies have estimated the relationship between single or multiple autoimmune diseases and associated environmental factors. There is limited information on the risk of various autoimmune diseases with respect to diseases caused by exposure to EAA.

Therefore, the primary aim of this study was to investigate whether exposure to EAA is associated with autoimmune disease based on data from the 2002–2019 National Health Insurance Service-National Sample Cohort (NHIS-NSC) database. In addition, we explored the density and distribution of each autoimmune disease according to the categorized exposure group to EAA.

2. Materials and methods

2.1. Study participants and sample collection

We used the NHIS-NSC dataset, a population-based cohort conducted by the NHIS of the Republic of Korea from 2002 to 2019 (Kweon et al., 2014). The NHIS provides mandatory public health insurance for approximately 98% of residents in the territory of Korea to cover medical care services, consistent with the policies of national health insurance, medical aid, and long-term care insurance. The NHIS-NSC dataset consists of medical services, qualifications, and medical check-up data that were intentionally masked. The medical service data included

records of all covered inpatient and outpatient visits, procedures, and prescriptions based on the standardized protocol of the Korea Classification of Diseases and Causes of Death, 4th edition, which corresponds to the International Classification of Diseases, 10th revision (ICD-10) (Organization, 2015).

The qualification data included age, sex, region, income, insurance type, identification number, and family information. The current study used 17,984,963 person-years from the NHIS-NSC, excluding 257,395 subjects who were diagnosed with autoimmune diseases before exposure to EAA from 18,242,358 person-years. Fig. 1 shows a detailed schematic diagram of the study population.

This study was performed in accordance with the ethical standards of the Declaration of Helsinki (1964) and its subsequent amendments. The NHIS-NSC data were anonymized before their release to the authors. All the participants provided written informed consent from the NHIS. The Institutional Review Board of the Gil Medical Center, Gachon University, approved this study (IRB number: GCIRB2021–380).

2.2. Autoimmune diseases categorization

Autoimmune diseases were categorized based on the InterLymph classification (Lee et al., 2020b). Inpatients with the following ICD-10 codes were included: sarcoidosis (D86), rheumatoid arthritis (M05.1–05.9, M06.0, and M08.0), systemic lupus erythematosus (M32 except for M32.0), dermatomyositis/polymyositis (M33), systemic sclerosis/scleroderma (M34 except for M34.2), Sjogren's syndrome (M35.0), Behcet's disease (M35.2), ankylosing spondylitis (M08.1 and M45), pernicious anemia (D51.0), autoimmune hemolytic anemia (D59.1), immune thrombocytopenic purpura (D69.38), Hashimoto's thyroiditis (E06.3), type I diabetes mellitus (E10), Grave's disease (E05.0), multiple sclerosis (G35), myasthenia gravis (G70.0), celiac disease (K90.0), ulcerative colitis (K51), Crohn's disease (K50), and psoriasis (L40). Based on the characteristics of the diseases, we classified them into two groups: connective tissue diseases and organ-specific diseases (Marrack et al., 2001).

2.3. EAA

It was difficult to define airborne dust exposure because of the nature of the dataset; therefore, it was necessary to define a group of people with suspected severe dust exposure according to previous studies (Wang et al., 2015; Lee et al., 2020a). The EAA exposure group was defined as patients who had visited a hospital facility as an inpatient and whose records included ICD-10 codes J6–7, 'Lung diseases due to external agents' by the World Health Organization. The EAA had the following 11 sub-codes: coal worker pneumoconiosis (J60); pneumoconiosis due to asbestos and other mineral fibers (J61); pneumoconiosis due to dust containing silica (J62); pneumoconiosis due to other inorganic dusts (J63); unspecified pneumoconiosis (J64); pneumoconiosis associated with tuberculosis (J65); airway disease due to specific organic dust (J66); hypersensitivity pneumonitis due to organic dust (J67); respiratory conditions due to inhalation of chemicals, gases, fumes, and vapors (J68); pneumonitis due to solids and liquids (J69);
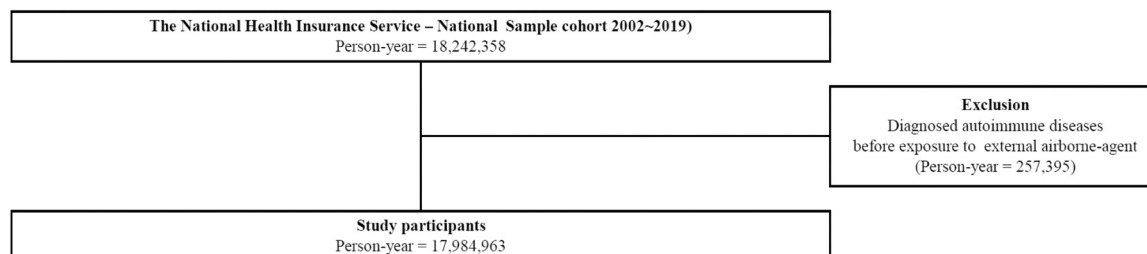

Fig. 1. The flow diagram of study participants.

and respiratory conditions due to other external agents (J70). The EAA group included inpatients who had J6–7 codes, but not the J65 or J69 sub-code. Both subcodes are generally used to describe lung diseases caused by factors other than airborne dust. Based on the characteristics of EAA, we classified them into three groups: inorganic dust exposure (J60, 61, 62, and 63), organic dust exposure (J66 and 67), and other dust exposure (J64, 68, and 70).

2.4. Statistical analysis

Baseline characteristics (sex, age, household income level, and EAA exposure) were described according to autoimmune diseases that were newly onset follow-up periods by chi-square test in the initial cohort. The incidence and rate ratio of autoimmune diseases according to EAA exposure to EAA was also demonstrated. The risk of autoimmune diseases according to the type of EAA exposure was estimated using logistic regression adjusted for age, sex, insurance type, and household income. The association between the type of autoimmune disease and type of EAA was described using a heatmap. All analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

The characteristics of the NHIS-NSC participants with and without autoimmune diseases are shown in Table 1. Of the 1,082,879 participants (546,936 men and 535,943 women), 86,376 (8.0%) had been diagnosed with autoimmune diseases, 36,186 (6.6%) were men, and 50,190 (9.4%) were women. Autoimmune diseases were more likely to occur in the older group, and 208 (14.1%) experienced severe EAA exposure.

Table 2 shows the status of all autoimmune diseases stratified by connective tissue and organ-specific diseases according to the exposure type. The rate ratio of total autoimmune diseases was 1.77 in participants who experienced exposure to EAA. Based on the categorized group of exposures, the rate ratio of total autoimmune diseases was 1.99 in the exposure to inorganic dust, 1.60 with organic dust exposure, and 1.68 with other dust exposure, respectively. After subgroup stratification, the rate ratios of connective tissue diseases were 1.86, 1.68, and 1.82 in exposure to inorganic dust, organic dust, and others, respectively. In addition, the rate ratios of organ-specific diseases were 2.06, 1.55, and 1.62 in exposure to inorganic dust, organic dust, and others, respectively.

In Fig. 2, we show the heat map to present the density and

Table 1
The characteristics of study participants of the National Health Insurance Service-National Sample Cohort according to autoimmune diseases.

		Autoimmune diseases, n (% of row)		P-value
		No	Yes	
Total participants		996,503 (92.0)	86,376 (8.0)	
Sex				<0.0001
	Men	510,750 (93.4)	36,186 (6.6)	
	Women	485,753 (90.6)	50,190 (9.4)	
Age (years at enrollment)				<0.0001
	<=20	409,450 (96.6)	14,352 (3.4)	
	21–40-	315,405 (92.0)	27,321 (8.0)	
	41–60	204,675 (86.9)	30,905 (13.1)	
	≥ 61	66,973 (82.9)	13,798 (17.1)	
Household income				0.1956
	Low	140,583 (91.5)	13,147 (8.5)	
	Low-Moderate	155,475 (92.0)	13,576 (8.0)	
	Moderate	185,305 (92.5)	15,067 (7.5)	
	Moderate-High	253,824 (92.6)	20,396 (7.4)	
	High	261,316 (91.5)	24,190 (8.5)	
External airborne-agent exposure				<0.0001
	No	995,239 (92.0)	86,168 (8.0)	
	Yes	1264 (85.9)	208 (14.1)	

Table 2
Status of autoimmune diseases according to type of external airborne-agent exposure.

		Autoimmune diseases, n (%, rate ratio)		
		Total	Connective tissue diseases	Organ-specific diseases
External airborne-agent exposure	Total	208 (14.1, 1.77)	70 (4.8, 1.82)	138 (9.4, 1.75)
	Inorganic	75 (15.9, 1.99)	23 (4.9, 1.86)	52 (11.0, 2.06)
	Organic	26 (12.8, 1.60)	9 (4.4, 1.68)	17 (8.3, 1.55)
	Others	107 (13.4, 1.68)	38 (4.8, 1.82)	69 (8.7, 1.62)

distribution of segmentalized autoimmune diseases according to each group of EAA. In the group of connective tissue diseases, rheumatoid arthritis occurred because of exposure to EAA. Among organ-specific diseases, psoriasis was distributed amongst almost all EAA. T1DM was found in most participants with coal worker pneumoconiosis or un-specified pneumoconiosis.

Table 3 presents the risk of autoimmune diseases according to EAA exposure using logistic regression analysis after adjusting for con-founding variables. Total EAA exposure was significantly associated with any autoimmune disease (OR: 1.29, 95% CI: 1.11–1.49) and organ-specific diseases (OR: 1.28, 95% CI: 1.08–1.53). Technically, although exposure to organic dust was not significantly associated with autoimmune diseases, inorganic dust exposure was associated with organ-specific diseases (OR: 1.38, 95% CI: 1.01–1.81). Exposure to other dust was significantly associated with any autoimmune disease (OR: 1.35, 95% CI: 1.10–1.66), connective tissue diseases (OR: 1.43, 95% CI: 1.03–1.99), and organ-specific diseases (OR: 1.28, 95% CI: 1.00–1.65).

4. Discussion

This study investigated the risk of autoimmune diseases caused by exposure to types of EAA. Our study found that the incidence of auto-immune diseases was increased in women and in the elderly. This consistent finding across previous studies highlights the importance of gender and age as significant factors influencing the occurrence of autoimmune diseases (Quintero et al., 2012).

Moreover, the incidence of autoimmune disease in individuals exposed to external airborne agents was 14.1%, indicating a 1.29 times higher risk of any types of autoimmune diseases than those who were not exposed to external airborne agents. The risk of organ-specific dis-eases was significantly associated with EAA exposure, including not only inorganic dust including asbestos, mineral, and metallic dust, but also other dust such as air pollution, chemicals, gases, fumes, and vapors, etc. Some scientific studies have suggested the plausible mechanisms that these could affect the autoimmune diseases. Entering these agents in human body, it can act as damage-associated molecular patterns to induce the occurrence of auto-inflammatory reactions, characterized by an increased flux of macrophages, increased production of inflammatory cytokines such as tumor necrosis factor, IL-1β and IL-6, and increased generation of reactive oxygen species. These activation lead to the stimulation of B cells and dendritic cells, resulting in the production of numerous antibodies and self-reactive T lymphocytes. It might be related to differences in the ability of target organs to resist autoimmune damage in different individuals (Zhao et al., 2019; Lissner et al., 2015; Ryu et al., 2019; Cao et al., 2022).

Our study also found that a significant relationship between the risk of connective tissue disease and exposure to other dust that may be exposed in daily living environments. Recent research suggests that exposure to environmental dust is linked to the progression of autoimmune diseases. Mechanisms included systemic inflammation,

		Connective tissue diseases								Organ specific diseases											
		Sarcoidosis	Rheumatoid arthritis	Systemic lupus erythematosus	Dermatomyositis/polymyositis	Systemic sclerosis/scleroderma	Sjogren's syndrome	Behcet's disease	Ankylosing spondylitis	Pernicious anemia	Autoimmune hemolytic anemia	Immune thrombocytopenic purpura	Hashimoto's thyroiditis	Type I diabetes mellitus	Grave's disease	Multiple sclerosis	Myasthenia gravis	Celiac disease	Ulcerative colitis	Crohn's disease	Psoriasis
Inorganic dust exposure	Coalworker pneumoconiosis	1	8	1	0	0	2	1	5	0	0	0	1	21	0	0	0	0	0	1	6
	Pneumoconiosis due to asbestos and other mineral fibres	0	2	0	0	0	0	0	1	0	0	1	3	2	0	0	0	0	0	0	5
	Pneumoconiosis due to dust containing silica	0	1	1	0	0	0	0	0	0	0	0	1	2	1	0	0	0	0	0	2
	Pneumoconiosis due to other inorganic dusts	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	1	0	2
Organic dust exposure	Airway disease due to specific organic dust	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0
	Hypersensitivity pneumonitis due to organic dust	0	6	1	0	0	0	1	0	0	0	0	0	3	2	0	0	0	2	2	7
Other dust exposure	Unspecified pneumoconiosis	0	13	0	0	1	2	1	2	0	0	0	1	22	1	0	0	0	1	1	11
	Inhalation of chemicals, gases, fumes, and vapours	0	5	0	1	0	1	1	5	0	0	0	3	8	0	0	0	0	3	1	9
	Respiratory conditions due to other external agents	0	4	0	0	0	1	1	0	0	0	1	0	0	0	1	0	0	1	0	5

Fig. 2. Heatmaps of the participants with external airborne-agent exposure and autoimmune diseases. The heatmap illustrates the association between the type of autoimmune disease and the EAA groups. The intensity of color represents the increased risk of association. The EAA groups are presented in the rows, classified as 'Lung diseases due to external agents' by the World Health Organization, including inorganic dust exposure, organic dust exposure, and others. On the other hand, autoimmune diseases are represented in the columns categorized based on the InterLymph classification and further divided into two groups based on their characteristics: connective tissue diseases and organ-specific diseases. The more vivid the color in the heatmap, the higher the association between each EAA group and autoimmune disease.

Table 3

Risk of autoimmune diseases according to type of external airborne-agent exposure.

		Autoimmune diseases, adjusted OR (95% CI)		
		Total	Connective tissue diseases	Organ-specific diseases
External airborne-agent exposure	Total	**1.29** **(1.11–1.49)**	1.25 (0.98–1.59)	**1.28** **(1.08–1.53)**
	Inorganic	1.20 (0.94–1.54)	1.03 (0.67–1.57)	**1.38** **(1.01–1.81)**
	Organic	1.29 (0.85–1.97)	1.23 (0.63–2.43)	1.29 (0.78–2.13)
	Others	**1.35** **(1.10–1.66)**	**1.43** **(1.03–1.99)**	**1.28** **(1.00–1.65)**

All results were adjusted age, sex, type of insurance, and household income.

heightened oxidative stress, epigenetic alterations, and immune responses triggered by airway damage. These can cause damage from multiple ways, not only attacking vulnerable organs, but also damaging the individual immune ecology, leading to a breakdown in immune tolerance. Thereby, to the development of systemic connective tissue disease (Zhao et al., 2019; Adami et al., 2021; Soleimanifar et al., 2019).

The noteworthy result to emphasize is that among various types of autoimmune diseases, RA, T1DM, and psoriasis was predominantly associated with exposure to EAA in this study. In several studies, it has been reported that exposure to inorganic dust, which serves as a direct cause of pneumoconiosis, is associated with an increased risk and severity of RA (Stolt et al., 2005; Min et al., 2021; Schmajuk et al., 2019). They can induce the activation of the NACHT, LRR, and PYD domain-containing protein 3 inflammasome and the production of IL-1, resulting in NF-κB activation and the release of proinflammatory cytokines such as IL-1β (Lee et al., 2017). Proinflammatory factors mediated

by inflammasomes lead to an imbalance between regulatory T cells and responder T cells, resulting in the occurrence of RA (Pollard, 2016).

Genetic predisposition is a recognized risk factor for T1DM; however, considering modification frequency of genetic risk factors is not paralleled by epidemiological trend changes, other risk factors could also contribute. Glands with secretory functions, such as the pancreas and thyroid, referred susceptible to environmental influences (Davies et al., 2020). Recent research reported that multiple exposure factors via environmental and occupational dust exposure have been proven to be associated with the onset of T1DM (Zhao et al., 2019; Zorena et al., 2022; Yun et al., 2022). It was indicated that exposure to airborne agents stimulates IL-1β and TNFα production in macrophages and pancreatic β cells, impairs pancreatic β cells, and inhibits the secretion of insulin in a dose-dependent manner in mice with T1DM (Zhang et al., 2021). Furthermore, some studies on the immune system have reported explainable mechanisms of immunometabolism. Exposure to mineral dust causes glycogen accumulation accompanied by nuclear translocation of NF-kB in macrophages through phagocytosis and glucose metabolic reprogramming of macrophages by single-cell RNA sequencing in lung tissue with pneumoconiosis (Wang et al., 2022). In addition, exposure to chemicals, gases, fumes, vapors, or other dust particles produces oxidative stress mediated by reactive oxygen species and can alter gene expression. These exposures can also lead to epigenetic modulation as part of the immune response by mechanisms such as DNA methylation in connective tissue diseases as well as organ-specific autoimmunity (Park et al., 2008; Di Dalmazi et al., 2016; Ogbodo et al., 2022; Marwa and Anjum, 2023).

Moreover, given that the skin is the largest organ directly exposed to EAA, persistent antigen exposure can destroy the skin barrier, cause chronic inflammatory reactions, and lead to skin tissue-specific autoimmune diseases. Psoriasis is a common dermatosis caused by uncontrolled keratinocyte proliferation and dysfunctional differentiation and

can be triggered or substantially aggravated by occupational risk factors that impair the skin barrier function (Rendon and Schäkel, 2019; Mahler et al., 2014).

To date, genetic and gender differences have been considered to have the greatest consequence on the development of autoimmune diseases. However, several studies have proven that environmental exposures can be risk factors for the immune system. This study raises important questions regarding the nature of EAA exposure and its effects on specific autoimmune diseases. To the best of our knowledge, this study is the first to investigate the association between EAA exposure and major autoimmune diseases in Koreans. The strength of our study is that it included a large sample size and a follow-up design, which allowed us to demonstrate the significant risk of autoimmune diseases associated with exposure to EAA. This study is valuable in that it is the first to examine the risk of autoimmune diseases according to EAA type. Our findings will be helpful for understanding the association between acquired airborne dust exposure and autoimmune disease risk.

However, this study had several limitations. We did not consider covariates, such as lifestyle and other autoimmune disease-related factors. Therefore, our results should only be interpreted in individuals who are exposed to severe airborne dust, which might be linked to an increased chance of visiting a medical facility due to autoimmune diseases. Our findings cannot be extrapolated to all individuals, because this was an ecological study. Furthermore, we defined autoimmune diseases using the ICD-10 codes in the NHS database, which may have had an undifferentiable misclassification error. However, according to a previous study that used the same definition of autoimmune diseases, this is considered reliable (Nemmar et al., 2014). The findings from current study were limited by the definition of exposure group. As noted, the NHIS-NSC database is based on national insurance system. We could not demonstrate the effect of occupational characteristics such as occupational classification, job duration, or job exposure matrix. Previous studies used similar definition of exposure group to describe various diseases risk under limited data, it could be a cornerstone study for next work, even not perfect (Lee et al., 2020a; Shin et al., 2022). Exposure to environmental dust such as PM10 or PM2.5 is also an important factor in the development of autoimmune disease. Although not addressed in this study the effect of environmental dust, future research should evaluate the impact of environmental dust and the combined exposure to occupational and environmental dust on risk of autoimmune disease.

In conclusion, this large retrospective cohort study revealed that the population exposed to EAA had an increased risk of autoimmune diseases. The association varied by autoimmune disease and specific exposure types. Further research is required to address the various autoimmune disease risks associated with dust exposure.

Funding

CRediT authorship contribution statement

Seunghyun Lee: Idea, Conceptualization, Research, Investigation, Analysis, Methodology, Verification, Writing – original draft, Writing – review & editing. **Xiaoxue Ma:** Idea, Conceptualization, Research, Investigation, Analysis, Methodology, Data curation, Writing – original draft, Writing – review & editing. **Wanhyung Lee:** Idea, Conceptualization, Analysis, Methodology, Funding acquisition, Project administration, Software, Simulation, Supervision, Verification, Writing – original draft, Writing – review & editing.

Author contributions

W.L. and S.L. designed the study and wrote the manuscript. S.L. and

X.M. contributed to data collection. S.L. and W.L. performed the statistical analysis and interpretation of the results. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Acknowledgments

References

Adami, G., et al., 2021. Association between environmental air pollution and rheumatoid arthritis flares. Rheumatology 60, 4591–4597. https://doi.org/10.1093/rheumatology/keab049.

Barragán-Martínez, C., et al., 2012. Organic solvents as risk factor for autoimmune diseases: a systematic review and meta-analysis. PLoS One 7, e51506. https://doi.org/10.1371/journal.pone.0051506.

Bengalli, R., et al., 2013. Release of IL-1β triggered by milan Summer PM 10: molecular pathways involved in the cytokine release. BioMed Res. Int. 2013 https://doi.org/10.1155/2013/158093.

Cao, Y., et al., 2022. TIM4/NLRP3 axis participates in the effects of M1 macrophages on inflammatory factor release, apoptosis and cell adhesion in thyroid follicular cells. Exp. Ther. Med. 24, 1–9. https://doi.org/10.3892/etm.2022.11615 eCollection 2022 Nov.

Celen, H., et al., 2022. Airborne pollutants as potential triggers of systemic autoimmune rheumatic diseases: a narrative review. Acta Clin. Belga 77, 874–882. https://doi.org/10.1080/17843286.2021.1992582.

Chen, H., et al., 2022. Effects of air pollution on human health–Mechanistic evidence suggested by in vitro and in vivo modelling. Environ. Res. 212, 113378 https://doi.org/10.1016/j.envres.2022.113378.

Conrad, N., et al., 2022. Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK. Lancet 400, 733–743. https://doi.org/10.1016/S0140-6736(22)01349-6.

Davies, T.F., et al., 2020. Graves' disease. Nat. Rev. Dis. Prim. 6, 52 https://doi.org/10.1038/s41572-020-0184-y.

Di Dalmazi, G., et al., 2016. Reactive oxygen species in organ-specific autoimmunity. Autoimmun. Highlights 7, 11. https://doi.org/10.1007/s13317-016-0083-0.

Kweon, S., et al., 2014. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int. J. Epidemiol. 43, 69–77. https://doi.org/10.1093/ije/dyt228.

Lee, S., et al., 2017. Silicosis and autoimmunity. Curr. Opin. Allergy Clin. Immunol. 17, 78–84. https://doi.org/10.1097/ACI.0000000000000350.

Lee, S., et al., 2020a. Effect of severe external airborne agents' exposure on dementia. J. Clin. Med. 9 https://doi.org/10.3390/jcm9124069.

Lee, W., et al., 2020b. External airborne-agent exposure increase risk of digestive tract cancer. Sci. Rep. 10, 8617. https://doi.org/10.1038/s41598-020-65312-6.

Lerner, A., et al., 2015. The world incidence and prevalence of autoimmune diseases is increasing. Int. J. Celiac Dis. 3, 151–155. https://doi.org/10.12691/ijcd-3-4-8.

Lissner, D., et al., 2015. Monocyte and M1 macrophage-induced barrier defect contributes to chronic intestinal inflammation in IBD. Inflamm. Bowel Dis. 21, 1297–1305. https://doi.org/10.1097/MIB.0000000000000384.

Mahler, V., et al., 2014. Psoriasis predisposition and occupational triggering factors in the appraisal of occupational medical expertises. J. Dtsch. Dermatol. Ges. 12, 519–529. https://doi.org/10.1111/ddg.12262.

Marrack, P., et al., 2001. Autoimmune disease: why and where it occurs. Nat. Med. 7, 899–905. https://doi.org/10.1038/90935.

Marwa, K., Anjum, F., 2023. Undifferentiated Connective Tissue Disease. StatPearls. StatPearls Publishing. Copyright © 2023, StatPearls Publishing LLC., Treasure Island (FL). PMID: 34283427, Bookshelf ID: NBK572061.

Min, Y.S., et al., 2021. Rheumatoid arthritis in silica-exposed workers. Int. J. Environ. Res. Public Health 18. https://doi.org/10.3390/ijerph182312776.

Mitratza, M., et al., 2021. Systemic autoimmune disease as a cause of death: mortality burden and comorbidities. Rheumatology 60, 1321–1330. https://doi.org/10.1093/rheumatology/keaa537.

Moroni, L., et al., 2012. Geoepidemiology, gender and autoimmune disease. Autoimmun. Rev. 11, A386–A392. https://doi.org/10.1016/j.autrev.2011.11.012.

Nemmar, A., et al., 2014. Pancreatic effects of diesel exhaust particles in mice with type 1 diabetes mellitus. Cell Physiol. Biochem. 33, 413–422. https://doi.org/10.1159/000356680.

Ogbodo, J.O., et al., 2022. Volatile organic compounds: a proinflammatory activator in autoimmune diseases. Front. Immunol. 13, 928379 https://doi.org/10.3389/fimmu.2022.928379.

Organization, W.H., 2015. Republic of Korea Health System Review. WHO Regional Office for the Western Pacific.

Park, H.J., et al., 2008. Time dependent gene expression changes in the liver of mice treated with benzene. Biomark. Insights 3, 191–201. https://doi.org/10.4137/BMI.S590.

Parks, C.G., et al., 1999. Occupational exposure to crystalline silica and autoimmune disease. Environ. Health Perspect. 107 (Suppl 5), 793–802. https://doi.org/10.1289/ehp.99107s5793.

Pollard, K.M., 2016. Silica, silicosis, and autoimmunity. Front. Immunol. 7, 97. https://doi.org/10.3389/fimmu.2016.00097.

Puustinen, P., et al., 2020. DNA-dependent protein kinase regulates lysosomal AMP-dependent protein kinase activation and autophagy. Autophagy 16, 1871–1888. https://doi.org/10.1080/15548627.2019.171043.

Quintero, O.L., et al., 2012. Autoimmune disease and gender: plausible mechanisms for the female predominance of autoimmunity. J. Autoimmun. 38, J109–J119 https://doi.org/10.1016/j.jaut.2011.10.003.

Rabbani, G., et al., 2023. Ever and cumulative occupational exposure and lung function decline in longitudinal population-based studies: a systematic review and meta-analysis. Occup. Environ. Med. 80, 51–60. https://doi.org/10.1136/oemed-2022-108237.

Rendon, A., Schäkel, K., 2019. Psoriasis pathogenesis and treatment. Int. J. Mol. Sci. 20 https://doi.org/10.3390/ijms20061475.

Ryu, Y.S., et al., 2019. Particulate matter induces inflammatory cytokine production via activation of NFκB by TLR5-NOX4-ROS signaling in human skin keratinocyte and mouse skin. Redox Biol. 21, 101080 https://doi.org/10.1016/j.redox.2018.101080. Epub 2018 Dec 15.

Schmajuk, G., et al., 2019. Prevalence of arthritis and rheumatoid arthritis in coal mining counties of the United States. Arthritis Care Res. 71, 1209–1215. https://doi.org/10.1002/acr.23874.

Shin, S., et al., 2022. Risk and status of gastrointestinal cancer according to the International Standard Industrial Classification in Korean workers. Cancers 14 (20), 5164. https://doi.org/10.3390/cancers14205164.

da Silveira Fleck, A., et al., 2021. Environmental and occupational short-term exposure to airborne particles and FEV1 and FVC in healthy adults: a systematic review and meta-analysis. Int. J. Environ. Res. Public Health 18, 10571. https://doi.org/10.3390/ijerph182010571.

Soleimanifar, N., et al., 2019. Effect of food intake and ambient air pollution exposure on ankylosing spondylitis disease activity. Adv. Rheumatol. 59, 9 https://doi.org/10.1186/s42358-019-0051-2.

Stolt, P., et al., 2005. Silica exposure is associated with increased risk of developing rheumatoid arthritis: results from the Swedish EIRA study. Ann. Rheum. Dis. 64, 582–586. https://doi.org/10.1136/ard.2004.022053.

Torén, K., et al., 2022. Cumulative occupational exposure to inorganic dust and fumes and invasive pneumococcal disease with pneumonia. Int. Arch. Occup. Environ. Health 95, 1797–1804. https://doi.org/10.1007/s00420-022-01848-6.

Wang, S.S., et al., 2015. Associations of non-Hodgkin Lymphoma (NHL) risk with autoimmune conditions according to putative NHL loci. Am. J. Epidemiol. 181, 406–421. https://doi.org/10.1093/aje/kwu290.

Wang, W., et al., 2022. Glycogen metabolism reprogramming promotes inflammation in coal dust-exposed lung. Ecotoxicol. Environ. Saf. 242, 113913 https://doi.org/10.1016/j.ecoenv.2022.113913.

Yun, B., et al., 2022. The relationship between occupational dust exposure and incidence of diabetes in male workers: a retrospective cohort study. Diabet. Med. 39, e14837 https://doi.org/10.1111/dme.14837.

Zhang, B., et al., 2021. PM(2.5) promotes β cell damage by increasing inflammatory factors in mice with streptozotocin. Exp. Ther. Med. 22, 832. https://doi.org/10.3892/etm.2021.10264.

Zhao, C.N., et al., 2019. Emerging role of air pollution in autoimmune diseases. Autoimmun. Rev. 18, 607–614. https://doi.org/10.1016/j.autrev.2018.12.010.

Zorena, K., et al., 2022. Air pollution, oxidative stress, and the risk of development of type 1 diabetes. Antioxidants 11. https://doi.org/10.3390/antiox11101908.