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Original Article

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Air Pollution Increases Healthcare Utilization Below Safe Thresholds in Individuals With Asthma

Hyun Lee [1,†] **Sang Hyuk Kim** [2,3†] **Sun-Kyung Lee** [1,4†] **Ji-Yong Moon** [5] **Kyung Hoon Min** [3] **Ho Joo Yoon** [1] **Sang-Heon Kim** [1*]

[1]Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea
[2]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Dongguk University Gyeongju Hospital, Dongguk University College of Medicine, Gyeongju, Korea
[3]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea
[4]Department of Mathematics, College of Natural Sciences, Hanyang University, Seoul, Korea
[5]Department of Internal Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Korea

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Correspondence to
Sang-Heon Kim, MD, PhD
Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, 222 Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea.
Tel: +82-2-2290-8336
Fax: +82-2-2298-9183
Email: sangheonkim@hanyang.ac.kr

[†]Hyun Lee, Sang Hyuk Kim, and Sun-Kyung Lee contributed equally to this work.

ORCID iDs
Hyun Lee
https://orcid.org/0000-0002-1269-0913
Sang Hyuk Kim
https://orcid.org/0000-0002-0410-8524
Sun-Kyung Lee
https://orcid.org/0000-0003-0033-1339
Ji-Yong Moon
https://orcid.org/0000-0003-2459-3448

ABSTRACT

Purpose: Safety thresholds for air quality levels have been proposed to protect people from the harmful effects of air pollutants. However, the impacts of air pollutants on asthma, particularly at levels below these safe thresholds, remain unclear.
Methods: We analyzed the associations between air pollutants (particulate matter of 10 μm or less in diameter [PM_{10}], particulate matter of 2.5 μm or less in diameter, sulfur dioxide [SO_2], carbon monoxide, ozone [O_3], and nitrogen dioxide) and healthcare utilization in 23,498 individuals with asthma in Seoul during the 2015–2017 season. The relative risk for healthcare utilization was assessed based on quantitative comparison (upper quartile vs. lower quartile) and non-linear concentration-response curves. Safety thresholds for air quality levels were determined according to the World Health Organization and Korean standards.
Results: In quantitative analysis, healthcare utilization risk decreased for PM_{10} and SO_2 but increased for O_3 on lag day 0, with no significant associations observed for other air pollutants. Non-linear analyses revealed significant concentration-response associations for all air pollutants, indicating increased risks of healthcare utilization on lag day 0. Notably, these increased risks occurred below proposed safety thresholds, with a steeper rise observed for asthma-related healthcare utilization within these ranges.
Conclusions: Exposure to 6 air pollutants was associated with an increased risk of healthcare utilization among individuals with asthma, with no safe exposure levels identified. The impact was more pronounced below current safety thresholds.

Keywords: Asthma; public health; environmental pollution; air pollution; particulate matter; threshold limit values

INTRODUCTION

Asthma is a heterogeneous lung disease characterized by chronic airway inflammation, often causing airflow limitation.[1] While many individuals with asthma maintain a stable

Kyung Hoon Min
https://orcid.org/0000-0003-0610-2182
Ho Joo Yoon
https://orcid.org/0000-0002-4645-4863
Sang-Heon Kim
https://orcid.org/0000-0001-8398-4444

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condition, a significant portion experience worsening of symptoms, necessitating more frequent healthcare use.[2] Thus, understanding the factors that contribute to uncontrolled asthma and more frequent healthcare use is crucial to improving asthma outcomes.[3] Of various factors, air pollution has gained attention as an important risk factor associated with uncontrolled asthma and more frequent healthcare use,[4,5] with growing interest in the global environmental crisis.[6,7]

Various air quality guidelines, including the Korean and World Health Organization (WHO) recommendations, present safe thresholds for air pollutants to protect people from the dangerous effects of these pollutants.[8,9] However, whether these thresholds can be applied to individuals with asthma is unclear. A previous study demonstrated that ambient particulate air pollution increased mortality, even at concentrations below the established safe threshold.[10] However, the analysis did not include other air pollutants, such as nitrogen dioxide (NO_2) and carbon monoxide (CO), nor did it assess their impact on individuals with specific comorbidities. Building on these findings, we hypothesize that air pollutants may also adversely affect healthcare utilization in individuals with asthma, even at levels considered safe.

In this study, we used population-level data to investigate the associations between air pollutant concentrations and healthcare utilization in individuals with asthma.

MATERIALS AND METHODS

Data source

We used the 2015–2017 Health Insurance Review and Assessment Service, National Patient Sample (HIRA-NPS), as our data source, which is a publicly accessible database representative of the national population.[11] This cross-sectional dataset includes health insurance claims from approximately 1.4 million people, representing a 3% stratified random sample based on age and sex. It provides detailed healthcare expenditures including both payer amounts and patient out-of-pocket costs. Our previous studies provided detailed information on this dataset.[12] This study was approved by the Institutional Review Board of Hanyang University Hospital (application No. HYUH 2022-08-043). Considering anonymization and the retrospective nature of HIRA-NPS data, informed consent from the participants to join the study was waived.

Study population

We initially obtained data from all individuals aged 20 years and older who utilized hospital services in Seoul, Korea, between January 1, 2015 and December 31, 2017. Of the initial 951,857 individuals, we excluded 928,359 without asthma. Finally, 23,498 individuals with asthma were included in the analytic cohort (**Fig. 1**).

Asthma

Asthma was defined by at least one claim under the 10th revision of the International Classification of Diseases (ICD-10) code J44–J45 and concurrent use of asthma medications including inhaled or oral corticosteroids, bronchodilators, leukotriene receptor antagonists, and xanthine derivatives.[13-16]

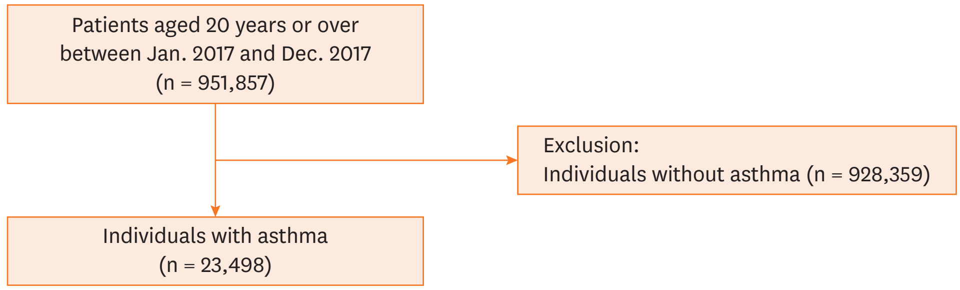

Fig. 1. Flow chart of the study.

Comorbidities

We identified comorbidities based on the ICD-10 codes.[17-30] The comorbidity conditions and their corresponding ICD codes are as follows: 1) chronic obstructive pulmonary disease (COPD): J42–J44 except J43.0, 2) a history of pulmonary tuberculosis: A15–A16, 3) cancers: C00–C97, 4) hypertension: I10–I15, 5) diabetes mellitus: E10–E14, 6) dyslipidemia: E78, and 7) cardiovascular disease (angina pectoris, myocardial infarction, or heart failure): I20 for angina pectoris, I21–I22, or I25.2 for myocardial infarction, and I43, I50, I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, or P29.0 for heart failure.

Measurements: meteorological and air pollution data

We received weather-related data from the Korea Meteorological Administration database for Seoul, which is located at a latitude of 37.57° N. This included metrics such as average temperature over 24 hours, humidity levels, and air pressure at sea level. Information regarding ambient air pollution levels was obtained from Air Korea (https://www.airkorea.or.kr), a publicly accessible database maintained by the Korean Ministry of the Environment.[9] Measurements of daily average pollutant concentrations were obtained from 25 observation sites across Seoul throughout the study period.

Air pollutants and air quality standards

We included air pollutants known to affect asthma.[4,31,32] These included large particulate matter with a diameter of 10 μm or less (PM_{10}) and small particulate matter with a diameter of 2.5 μm or less ($PM_{2.5}$). In addition, the gaseous pollutants sulfur dioxide (SO_2), CO, ozone (O_3), and NO_2 were included. The standards for air quality assessment were derived from both the WHO and Korean national air quality standards (**Supplementary Table S1**).[8]

Study outcome

The outcome of this study was all-cause healthcare utilizations, including outpatient department visits, emergency room visits, and hospitalization. To account for different healthcare utilization patterns on weekends and holidays, healthcare utilization from these days was excluded.

Statistical analysis

Categorical variables were expressed as numbers with percentages. The relative risk for healthcare utilization according to concentrations of air pollutants was assessed as follows: 1) comparing the lower quartile (Q1) to the upper quartile (Q3) in each pollutant and 2) concentration-response curves with the lowest level of pollutants as references. For concentration-response curves, a Generalized Additive Model with a Poisson distribution was used to analyze the associations between air pollutant levels and healthcare utilization.

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Risk ratios were calculated per 1 unit increase, using the lowest pollutant concentration as the reference. Smoothing splines were also included to manage variations in the Generalized Linear Model equation and degrees of freedom were determined based on the lowest Akaike's information criterion value for optimal model fit. This approach allows stable estimation across varying population sizes and distributions, even when data are sparse in some part of the graph. For all analyses, we adjusted for seasonal variations to account for factors that may influence healthcare utilization among individuals with asthma. In addition, natural cubic splines were employed to adjust for non-linear confounding factors, such as daily average temperature and the daily average relative humidity. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA) and R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics

The **Table** provides the baseline characteristics of the study population. The individuals were distributed relatively evenly across all age groups; the largest proportion was 20.8% for those in their 70s, and the smallest proportion was 10.9% for those in their 20s. Most individuals had self-employed health insurance (94.2%). Regarding respiratory comorbidities, the proportions of individuals with comorbid COPD and a history of pulmonary tuberculosis were 18.7% and 0.8%, respectively. The most common comorbidity was dyslipidemia (42.6%), followed by hypertension (34.9%), diabetes mellitus (22.8%), cardiovascular disease (10.0%), and cancers (7.9%).

Air pollutants and meteorological data

As shown in **Supplementary Table S2**, the median concentrations of air pollutants during the study period were as follows: PM_{10} at 44.5 μg/m^3, $PM_{2.5}$ at 22.5 μg/m^3, NO_2 at 0.037 parts

Table. Baseline characteristics of the study population

Variables	Total (n = 23,498)
Age (yr)	
20–29	2,559 (10.9)
30–39	3,585 (15.3)
40–49	3,538 (15.1)
50–59	4,383 (18.7)
60–69	4,518 (19.2)
≥ 70	4,915 (20.8)
Sex	
Male	8,754 (37.3)
Female	14,744 (62.7)
Type of insurance	
Self-employed health insurance	22,128 (94.2)
Employee health insurance	1,176 (5.0)
Medical aid	194 (0.8)
Comorbidities	
COPD	4,383 (18.7)
History of pulmonary tuberculosis	182 (0.8)
Cancers	1,850 (7.9)
Hypertension	8,204 (34.9)
Diabetes mellitus	5,347 (22.8)
Dyslipidemia	10,008 (42.6)
Cardiovascular disease	2,340 (10)

Values are presented as numbers (%).
COPD, chronic obstructive pulmonary disease.

per million (ppm), SO_2 at 0.004 ppm, O_3 at 0.019 ppm, and CO at 0.532 ppm. The median temperature and humidity were 14.6°C and 59.0%.

Quantitative analysis for air pollutants and healthcare utilization

When comparing the 3Q to the 1Q of PM_{10} and SO_2, the risk of healthcare utilization decreased, while the risk increased with the 3Q compared to the 1Q of O_3, both on lag day 0. However, no significant changes were observed for other air pollutants (**Fig. 2**). PM_{10}, and $PM_{2.5}$ exhibited a peak-and-plateau pattern, with a gradual increase in risk ratios peaking around lag day 4. NO_2, SO_2, and CO showed a steadily increasing trend, reaching higher values by lag day 7. In contrast, O_3 displayed a decreasing trend in risk ratios over the lag days.

Non-linear association between air pollutants and healthcare utilization

The concentration-response curves demonstrated a significant association between all air pollutants and increased healthcare utilization at lag day 0 (**Fig. 3**). The highest risk ratios were observed on lag day 0 for PM_{10}, $PM_{2.5}$, SO_2, and CO. In contrast, NO_2 consistently showed elevated risk ratios regardless of lag day. For O_3, slightly increased risk ratios were observed on lag days 0 and 7, but overall, the ratios tended to decrease. Notably, the increased healthcare utilization associated with all air pollutants occurred at concentrations below the air quality standards set by both the WHO and Korea. The 95% confidence intervals of the non-linear analyses are presented in **Supplementary Fig. S1**.

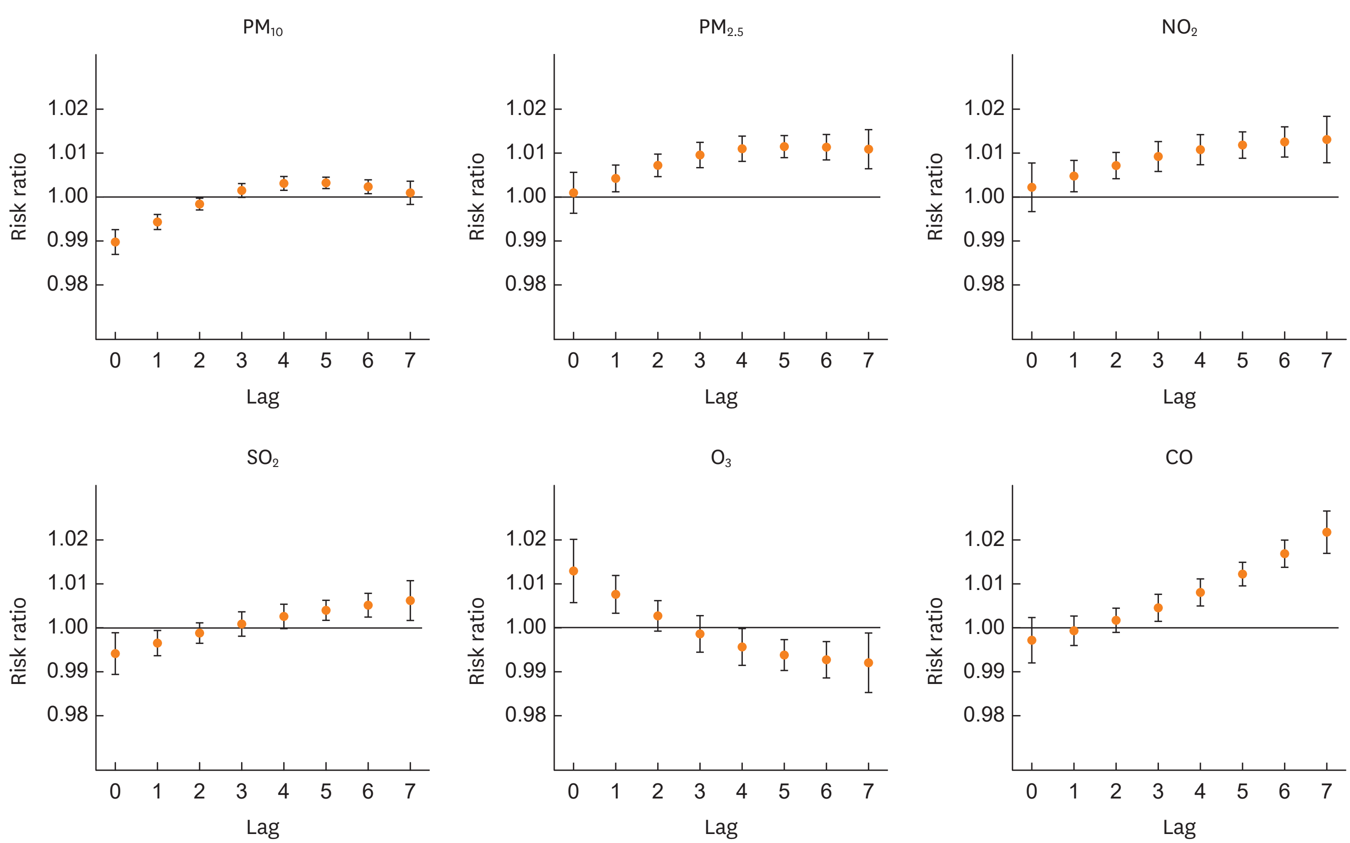

Fig. 2. Associations between air pollutants and healthcare utilization comparing upper and lower quartile levels of air pollutants.
PM_{10}, particulate matter of 10 µm or less in diameter; $PM_{2.5}$, particulate matter of 2.5 µm or less in diameter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; CO, carbon monoxide.

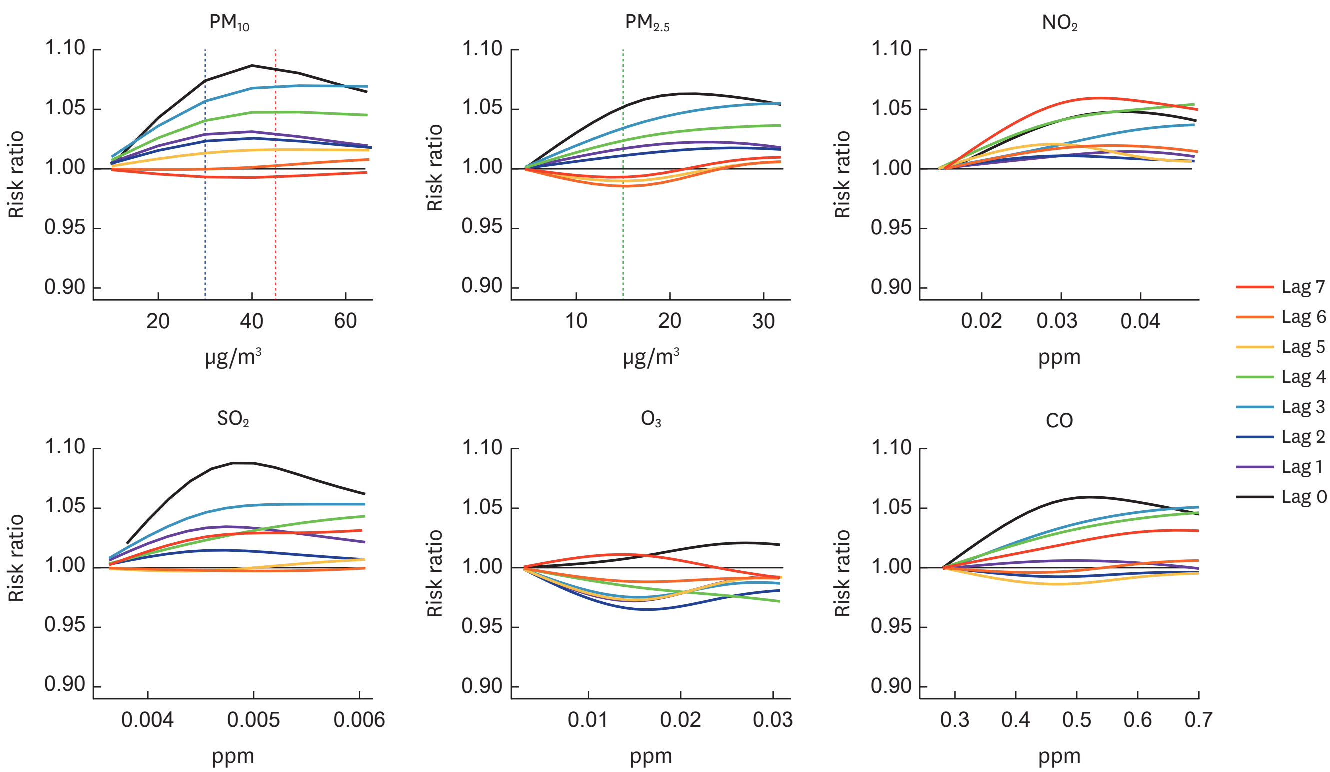

Fig. 3. Concentration-response curves for the associations between air pollutants and healthcare utilization in individuals with asthma. Blue, red, and green vertical dashed lines indicate the Korean, World Health Organization, and shared standard levels for good air quality of particulate matter, respectively. The standard levels for other pollutants were based on 8-hour or 1-hour average concentrations, limiting direct comparison.
PM_{10}, particulate matter of 10 μm or less in diameter; $PM_{2.5}$, particulate matter of 2.5 μm or less in diameter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; CO, carbon monoxide.

DISCUSSION

This 3-year study on healthcare utilization among individuals with asthma in Seoul found that all assessed pollutants—PM_{10}, $PM_{2.5}$, NO_2, SO_2, CO, and O_3, were significantly associated with increased healthcare utilization, even at concentrations below the recommended air quality standards.

The adverse effects of air pollution, particularly $PM_{2.5}$, NO_2, and O_3, on asthma have been continuously reported.[4,31] Even short-term exposure to these air pollutants can worsen asthma control status.[33,34] Complementing these findings, our results revealed that all major air pollutants (in non-linear analyses) increased the risk of healthcare utilization in individuals with asthma, especially on the day of exposure (day 0). This adds to the evidence of the harmful effects of short-term exposure to these pollutants on asthma control. We also showed that these effects could persist for up to about 1 week in NO_2, suggesting the importance of the delayed impacts of exposure to air pollutants.

Several harmful mechanisms of air pollutants for asthma were proposed. PM is implicated in direct damage to the airway epithelium, leading to mucosal edema, and is associated with dysfunction in airway macrophages.[35] NO_2, SO_2, and O_3 induce airway inflammation, a process mediated through the release of various cytokines, including interleukin-8 and tumor necrosis factor-beta.[36,37] Moreover, environmentally persistent free radicals, particularly those linked to PM, NO_2, and O_3 exposure, could exacerbate asthma.[38-40] NO_2 and O_3 exposure are also associated with the induction of airway hyper-responsiveness in individuals with asthma.[41,42] While the impact of CO on asthma is less well-defined, a reduction in lung function has been observed in individuals with asthma following CO exposure.[43] In summary, these air pollutants could exacerbate asthma via multiple pathways of airway epithelial damage, increased airway inflammation, linkage with environmentally persistent free radicals, and induction of airway hyper-responsiveness.

Several studies have investigated the association between air pollution and healthcare utilization using similar datasets to ours. Song *et al.*[44] found that PM levels exceeding the standard thresholds were associated with increased asthma-related hospital visits. Lee *et al.*[45] reported a linear association between PM_{10}, $PM_{2.5}$, NO_2, CO, and SO_2 and asthma-related healthcare utilization. However, neither study focused on the impact of air pollution below the currently suggested thresholds. Although Wei *et al.*[46] demonstrated that increased levels of air pollution below the U.S. standard thresholds can lead to more frequent hospital admissions among individuals with asthma, it was unclear whether the impact was more pronounced below the thresholds. We found that a steeper increase in asthma-related healthcare utilization risk was observed below the thresholds for most air pollutants using a non-linear analysis. Recognizing that no level of air pollution is safe for asthma, a holistic approach to asthma management is imperative.[47]

Clinicians should play a key role in this strategy by educating individuals with asthma about the risks associated with any level of air pollution, emphasizing that detrimental effects can occur and may increase even more significantly below the currently suggested thresholds. Proactive adjustment of medications during high air pollution seasons should also be considered. Although no specific preventive medications are currently recommended, these adjustments might include a preemptive increase in inhaled corticosteroid dosage or the addition of controller medications tailored to an individual's condition. Personal protective methods, such as wearing facial masks, should also be strongly encouraged.[48] Health policies and air pollution guidelines for individuals with asthma are needed since the current air quality guidelines cannot be applied to this population.

In our quantitative analyses, only high levels of O_3 were associated with an increased risk of healthcare utilization in individuals with asthma, contrasting with findings from non-linear analyses. Specifically, higher levels of PM_{10} were associated with a decreased risk of healthcare utilization on lag day 0. Additionally, for PM_{10}, $PM_{2.5}$, NO_2, and SO_2, the risk of healthcare utilization increased as lag days progressed. This may be due to the narrow distribution of air pollution levels in Korea, where the gap between lower and upper quantiles may not be substantial enough to capture the full impact of air pollutants. Therefore, when evaluating the effects of air pollution on asthma at a population level, non-linear analyses may provide a more comprehensive perspective than those based solely on quantitative assessments of air pollutants.

The limitations of this study should be considered. First, the diagnosis of asthma was primarily determined using ICD-10 codes, which could lead to under- or overdiagnosis.[49] Secondly, some important clinical data related to asthma, such as lung function measurements and eosinophil counts in the blood or sputum, were not considered due to their absence from our dataset.[50] Thirdly, the analysis could not account for potential confounding factors, such as residential area, major road proximity, upper respiratory infections, and occupational exposure. Fourthly, we did not assess the potential interactions between various air pollutants. Finally, the results of this study should be generalized cautiously since this study was conducted in a single city within a single nation.

In conclusion, exposure to 6 air pollutants was associated with an increased risk of healthcare utilization among individuals with asthma, with no safe exposure levels identified. The impact of increased air pollution on healthcare utilization was more pronounced below current safety thresholds. Considering the undeniable impact of air pollution on asthma, it is imperative to adopt a holistic approach to asthma management, recognizing that no level of air pollution is safe in this population.

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SUPPLEMENTARY MATERIALS

Supplementary Table S1

Recommended air pollutant limits in air quality guidelines

Supplementary Table S2

Statistical summary of air pollutants and meteorological data in Seoul during the study period

Supplementary Fig. S1

95% confidence intervals of the non-linear analyses.

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