

Low-to-moderate atmospheric ozone levels are negatively correlated with hospital visits by asthma patients

Soyeon Lee, BSN^a, Minhyeok Lee, PhD^{a,*} 

Abstract

Asthma is a chronic illness of the airways that affects approximately 300 million individuals worldwide. While it is commonly accepted that high ozone levels exacerbate asthma symptoms, the impact of low to moderate ozone levels on asthma symptoms has received little attention. The purpose of this research was to determine the relationship between hospital visits by asthma patients showing the severity of their symptoms and moderate ozone levels. Statistical analyses were performed on hospital visit big data for asthma patients in Seoul, Korea, collected between 2013 and 2017. The data set includes outpatient hospital visits ($n = 17,787,982$), hospital admissions ($n = 215,696$), and emergency department visits ($n = 85,482$). The frequency of hospital visits by asthma patients was evaluated in relation to low ozone levels (< 0.03 ppm) and moderate ozone levels (0.03 – 0.06 ppm) in the Seoul environment. In comparison to low ozone levels, moderate ozone levels resulted in a reduction in outpatient hospital visits ($t = 7.052$, $P < .001$). When ozone levels were low to moderate, there was a negative correlation between ozone levels and outpatient visits ($r = -0.281$, 95% CI: -0.331 to -0.228). Negative associations were also identified between ozone levels and new hospital admissions ($t = 2.909$, $P < .01$; $r = -0.125$, 95% CI: -0.179 to -0.070) and emergency treatments ($t = 2.679$, $P < .01$; $r = -0.132$, 95% CI: -0.186 to -0.076). Additionally, it was verified that moderate ozone levels one day before the visits resulted in a reduction in outpatient visits ($t = 5.614$, $P < .001$; $r = -0.207$, 95% CI: -0.259 to -0.153). A strong relationship was identified between moderate atmospheric ozone levels and a reduction in asthma patient hospital visits.

Keywords: asthma, atmospheric ozone, big data analysis, hospital visits, national health insurance database, retrospective study

1. Introduction

Asthma is a chronic respiratory condition characterized by inflammation of the airways, chest discomfort, wheezing, coughing, and trouble breathing.^[1–3] Asthma is so prevalent that it has been estimated that nearly 300 million individuals globally suffer from the disease.^[4,5] Air pollution is a well-known cause of asthma since it triggers allergic responses in the airways.^[6–8] Numerous forms of atmospheric pollutants, such as NO₂, carbon monoxide, CO₂, SO₂, and ozone (O₃), have been shown to have a substantial correlation with asthma occurrences and exacerbations.^[9–17]

It has been extensively observed that elevated ozone levels have an inflammatory impact on the respiratory system, which likely contributes to the progression of asthma.^[12,18,19] The connection between low to moderate ozone levels and asthma, on the other hand, has received less attention. The goal of this research is to investigate associations between

low to moderate ozone levels and asthma utilizing hospital visit data from 2013 to 2017 for asthma patients in Seoul, Korea. This research examined approximately 18 million hospital visits, admissions, and emergency department visits for asthma patients in Seoul on a daily basis with the atmospheric ozone levels.

2. Materials and methods

2.1. Hospital visit database for asthma patients in Seoul

The legislation requires the Korean people to have national health insurance. As a result, the National Health Insurance Service of Korea has acquired all medical data of Korean citizens. National Health Insurance Service has produced a hospital visit database for asthma patients in Korea that includes daily outpatient hospital visits, hospital admissions, and emergency department visits.

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The authors declare no conflict of interest.

The datasets generated during and/or analyzed during the current study are publicly available.

Ethical review was waived for this study with the approval of Chung-Ang University IRB (No. 1041078-202201-HR-047) due to the retrospective nature of the study and the publicly available datasets used in this study.

^a School of Electrical and Electronics Engineering, Chung-Ang University, Seoul, Korea.

* Correspondence: School of Electrical and Electronics Engineering, Chung-Ang University, Seoul, Korea (e-mail: mlee@cau.ac.kr).

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Seoul is the capital city of South Korea, with a population of around ten million. This research studied asthma patients in the Seoul area using the database. Approximately 26 million cases of hospital visits of asthmatic patients were admitted in Seoul between 2013 and 2017, according to the database. In this study, weekend records were excluded since they showed a different trend than weekdays due to closed hospitals. Additionally, data for 63 Korean national holidays from 2013 to 2017 were omitted for the same reason. The hospital visits were log-normalized in order to convert the data distributions to Gaussian distributions for statistical analysis. Figure 1 depicts a high-level overview of the database preparation process.

2.2. Daily atmospheric ozone concentration database

This research employed a daily atmospheric ozone concentration database to determine the ground-level ozone level at 25 locations in Seoul. For each date, the data collected at each point were averaged. The median ozone concentration was 0.022 ppm, whereas the highest and lowest values were 0.002 ppm and 0.071 ppm, respectively. Figure 2 depicts the spread of ozone concentrations over the days from 2013 to 2017 in Seoul. Weekends and national holidays were also omitted from the data in accordance with the hospital database. As a result, although most of the days in the experimental period belong to low to moderate ozone levels, the low ozone

levels (less than 0.03 ppm) and moderate ozone levels (0.03–0.06 ppm) were distinguished by a threshold of 0.03 parts per million. Thus, 914 days and 323 days correspond to low ozone levels and moderate ozone levels, respectively, throughout the experimental period.

2.3. Statistical analyses

The Welch’s *t* test was performed to determine the difference in hospital visits between low and moderate ozone levels. Pearson correlation coefficients were calculated for ozone levels ranging from low to moderate (< 0.06 ppm) in order to determine the influence of ozone levels on hospital visits. Independently, outpatient hospital visits, hospital admissions, and emergency department visits were evaluated for ozone levels. The relationships with ozone levels on the same day as the visits and with ozone levels one day prior to the visits were evaluated separately. R version 4.1.2 was used for statistical analysis, with *p* values less than .05 deemed significant.

2.4. Institutional review board statement

Ethical review was waived for this study with the approval of Chung-Ang University IRB (No. 1041078-202201-HR-047) due to the retrospective nature of the study and the publicly accessible datasets used in this study.

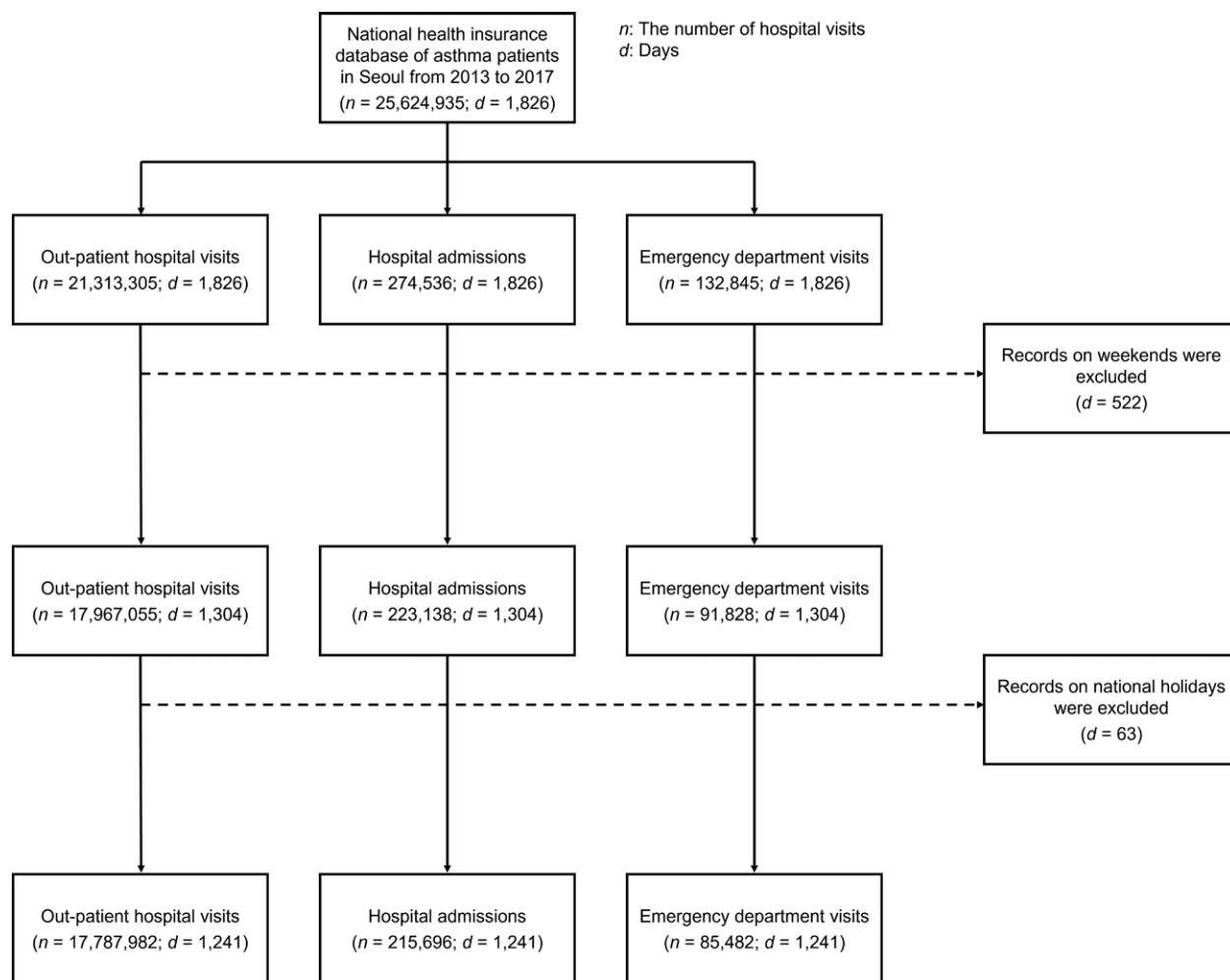


Figure 1. Preprocessing procedures for the database used in this study.

3. Results

3.1. Associations between outpatient hospital visits and atmospheric ozone levels

The frequency of outpatient hospital visits by asthma patients reduced significantly when their ozone levels were moderate ($t = 7.052, p < .001$). The frequency of outpatient hospital visits reduced as ozone levels rose, resulting in a negative association ($r = -0.281, 95\% \text{ CI: } -0.331 \text{ to } -0.228, p < .001$). The distributions of the number of visits with respect to ozone levels are shown in Fig. 3. Significant hospital visit changes in ozone levels between 0 ppm and 0.01 ppm ($p < .001$), 0.02 ppm and 0.03 ppm ($p < .001$), and 0.03 ppm and 0.04 ppm ($p = .018$) were detected across the groups.

3.2. Associations between hospital admissions and atmospheric ozone levels

The number of new hospital admissions of asthma patients decreased in moderate ozone levels compared to low ozone levels ($t = 2.909, p < .001$). The number of new hospital admissions decreased as the ozone levels increased, exhibiting a negative correlation ($r = -0.125, 95\% \text{ CI: } -0.179 \text{ to } -0.070, p < .001$). The distributions of the number of admissions with respect to ozone levels are shown in Fig. 4.

Discrepancies in the number of admissions were shown between the groups of ozone levels of 0 ppm and 0.01 ppm ($p = .022$), as well as 0.02 ppm and 0.03 ppm ($p = .031$).

3.3. Associations between emergency department visits and atmospheric ozone levels

Moderate ozone levels showed fewer emergency department visits of asthma patients compared to low ozone levels ($t = 2.679, p < .001$). The ozone levels and the number of emergency department visits exhibited a negative correlation ($r = -0.132, 95\% \text{ CI: } -0.186 \text{ to } -0.076, p < .001$). The distributions of the number of visits regarding ozone levels are described in Fig. 5. A significant difference was observed between the groups of ozone levels of 0 ppm and 0.01 ppm ($p = .017$).

3.4. Associations between outpatient hospital visits and atmospheric ozone levels 1 day prior to the visits

The relationship between the number of hospital visits and ozone levels one day before the visits was investigated. It was confirmed that moderate ozone levels of the previous day are likely to reduce the number of visits compared to low ozone levels ($t = 5.614, P < .001$). It was demonstrated that the number of hospital visits and ozone levels of the previous day were

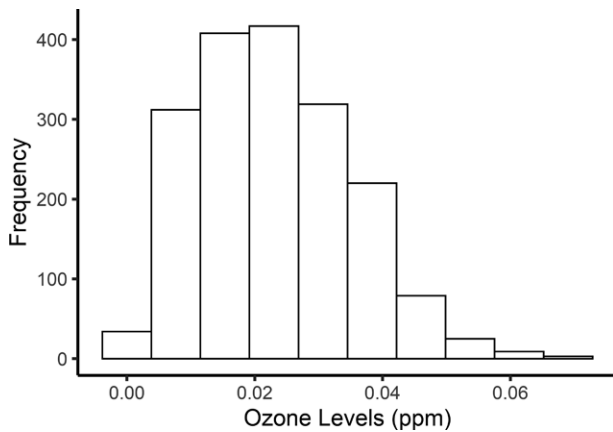


Figure 2. Distribution of average daily ozone levels of Seoul from 2013 to 2017.

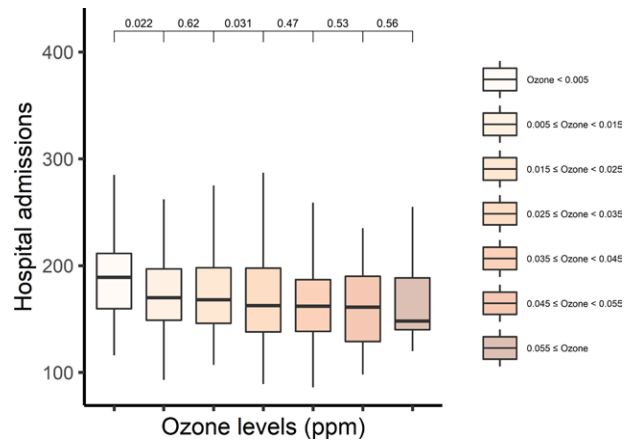


Figure 4. The number of hospital admissions by asthma patients with respect to ozone levels.

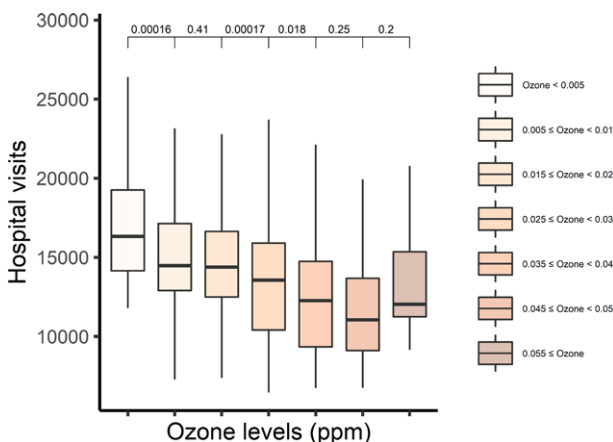


Figure 3. The number of outpatient hospital visits by asthma patients with respect to ozone levels.

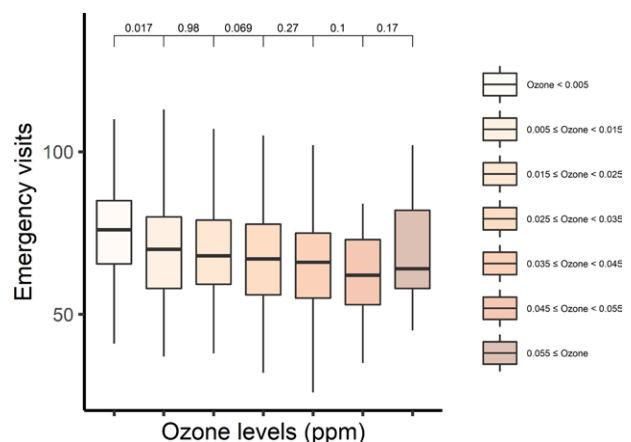


Figure 5. The number of emergency department visits by asthma patients with respect to ozone levels.

negatively correlated ($r = -0.207$, 95% CI: -0.259 to -0.153 , $P < .001$). The distributions of the number of visits with respect to ozone levels are shown in Fig. 6. Significant differences were exhibited between the groups of ozone levels of 0 ppm and 0.01 ppm ($P < .01$), as well as 0.02 ppm and 0.03 ppm ($P < .001$).

3.5. Subgroup analyses

To examine the effect of the moderate levels of ozone on each subgroup in the database, additional research was undertaken in relation to sex and age. Table 1 provides the results. Consequently, outpatient visits were strongly negatively associated in all subgroups, with correlation coefficients below -0.2 and t test p values below .0001. This finding shows that moderate ozone levels reduced the number of outpatient visits compared to low ozone levels, regardless of the subgroup.

For hospital admissions and emergency visits, however, significant correlations were observed only in the subgroups of

females and those under 19 years of age, whereas the other subgroups did not demonstrate a significant correlation between low-to-moderate ozone levels and visits.

4. Discussion

This study established a negative correlation between ozone levels in the atmosphere and the frequency of hospital visits by asthma patients when ozone levels are not at high levels. Numerous studies have demonstrated a connection between high ozone levels and asthma,^[11,18–20] but the potential of this study is interesting because it establishes a negative correlation between asthma and low to moderate ozone levels. In this study, it was demonstrated that an increase in ozone concentration does not always impact asthma patients, as moderate ozone levels resulted in fewer asthma patient hospital visits when compared to low ozone levels.

Several studies have explored the associations between high ozone levels and asthma. Population-based studies have shown that asthmatics are more vulnerable to poor air quality, and this relationship may be explained by a variety of processes. The initial impact seems to be temporary and is mediated via the nervous system. There seems to be a delayed effect associated with air pollution, particularly with ozone.^[21–23] Lung function changes after ozone exposure are related to an exaggerated inflammatory response in the airways. This reaction is amplified in persons with asthma, with both neutrophils and eosinophils infiltrating the airways.^[24,25] Additionally, pre-exposure to ozone enhances the asthmatic response to inhaled allergen.^[26,27]

According to several papers, there is a time lag between higher ozone levels and their consequences, and the development of inflammatory responses as a result of ozone exposure might occur during such a time lag.^[18,21–23,28] Additionally, one research discovered a statistically significant relationship between emergency department visits and average ozone saturation levels on the day of admission, as well as on days 2 and 3.^[29] These investigations motivated us to study the relationship between 1-day delayed hospital visits and ozone levels. In contrast to

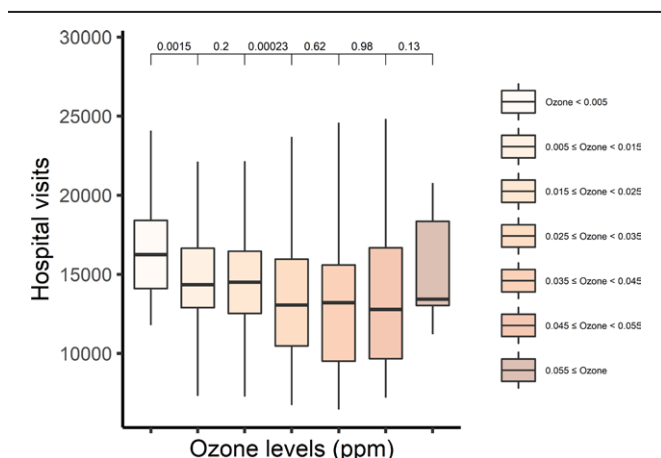


Figure 6. The number of outpatient hospital visits by asthma patients with respect to ozone levels one day prior to the visits.

Table 1

Subgroup analyses with respect to sex and age.

Subgroup	Events	Correlation Coef.	95% CI	P value (t test)
Outpatient	17,787,982			
Sex				
Male	8290,785	-0.272	(-0.323, -0.220)	<.0001
Female	9497,197	-0.286	(-0.336, -0.234)	<.0001
Age				
0 – 19	7920,891	-0.267	(-0.318, -0.214)	<.0001
20 – 59	5065,012	-0.286	(-0.337, -0.234)	<.0001
60+	4802,079	-0.216	(-0.269, -0.163)	<.0001
Admission	215,696			
Sex				
Male	111,875	-0.078	(-0.133, -0.023)	.147
Female	103,821	-0.156	(-0.209, -0.101)	<.0001
Age				
0 – 19	59,369	-0.194	(-0.247, -0.140)	<.0001
20 – 59	38,365	-0.055	(-0.110, -0.001)	.340
60+	117,962	-0.031	(-0.087, -0.024)	.343
Emergency	85,482			
Sex				
Male	47,105	-0.057	(-0.112, -0.001)	.396
Female	38,377	-0.179	(-0.233, -0.125)	<.0001
Age				
0 – 19	24,899	-0.135	(-0.189, -0.189)	<.001
20 – 59	15,728	-0.033	(-0.088, -0.088)	.906
60+	44,855	-0.059	(-0.115, -0.004)	.256

the majority of previous investigations, our study found that increase in atmospheric ozone levels did not result in an increase in the number of hospital visits, hospital admission, and emergency department visits for the present day and 1-day delays. These findings may be explained by the fact that the average ozone levels in this study were at low to moderate levels, in which the highest level in the database was 0.071 ppm, while ozone concentrations in previous investigations were at high levels with a minimum of 0.1 ppm.

Despite the distinct demonstration of the relationship in this study, a better understanding of why a moderate ozone concentration can reduce hospital visits by asthma patients should be carried out, although one possibility is that the antibacterial and antiviral characteristics of ozone help to reduce the source of asthma-related complications. Plentiful studies have been done on the antibacterial and antiviral properties of ozone, and numerous of these studies report the use of ozone in the treatment of bacterial and viral infections.^[30–32] For instance, one research discovered that a single topical treatment of a small amount of ozone supplied by nebulization completely prevented the growth of all potentially hazardous bacterial strains previously known to be resistant to antimicrobial drugs.^[33] A study found that ozone-oxygen mixture therapy was demonstrated to have the potential to be a successful treatment for COVID-19 patients with severe respiratory failure.^[34] A thorough review paper elaborated that ozone treatment seems to be effective in reducing inflammation, activating immunity as well as antiviral activity, and protecting against acute coronary syndromes and ischemia–reperfusion damage, indicating a novel immunotherapeutic paradigm.^[35] Given ozone-based treatments for these respiratory diseases and bacteria, it may also be possible to explore the effect of mild atmospheric ozone on bacteria and viruses since these bacterial and viral respiratory infections exacerbate asthma symptoms.

There are a few limitations to the findings of this study. It was not taken into consideration any other atmospheric parameters such as temperature, humidity, weather, or concentrations of other air-polluting particles such as nitrogen dioxide, nitrogen monoxide, CO, carbon dioxide, or SO₂. Because of the limitations of the database, no subgroup analyses of asthma patients were undertaken based on severity of their asthma. There is a possibility that the number of hospital visits is not directly related to the severity of the symptom. Regardless of the constraints of these investigations, since it is established that a large number of samples and a lengthy search time may mitigate these limits, the conclusions of this research can be stated to have been shown by statistical analyses in this study.

Author contributions

Conceptualization: Soyeon Lee, Minhyeok Lee.

Formal analysis: Soyeon Lee.

Investigation: Soyeon Lee, Minhyeok Lee.

Methodology: Soyeon Lee, Minhyeok Lee.

Software: Soyeon Lee.

Supervision: Minhyeok Lee.

Validation: Soyeon Lee.

Writing—original draft: Soyeon Lee, Minhyeok Lee.

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