

Association Between Particulate Matter Pollutants and Ophthalmology Visits for Ocular Surface Irritation and Allergy

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Background: The World Health Organization has declared climate change to be “the single biggest health threat facing humanity”, yet there are limited studies on the impact of climate change-related air pollution on ocular health.

Objective: To explore associations between ocular surface irritation and allergy-related daily outpatient office visits with daily ambient particulate matter (PM) levels in the Denver Metropolitan Area.

Methods: Daily visit counts of ophthalmology outpatient offices were obtained from an academic health center (October 1st, 2015 to January 27th, 2023). Daily ambient average concentrations of PM $\leq 10 \mu\text{m}$ in diameter (PM₁₀) and 2.5 micrometers or less in diameter (PM_{2.5}) were obtained. Data were analyzed using distributed lag nonlinear models while accounting for the cumulative lagged effects of PM₁₀ and PM_{2.5} for visits. Modifications due to temperature were assessed using stratified models.

Results: There were 144,313 ocular surface irritation and allergy visits to ophthalmic clinics during the study period. Daily visit counts increased with increasing daily ambient PM₁₀ and PM_{2.5} concentrations. Five-day cumulative ambient PM₁₀ concentrations at 80, 90, 100, and 110 $\mu\text{g}/\text{m}^3$ showed higher rate ratios at each level from 1.77 (95% CI: 1.71, 1.84) at concentration of 80 to 2.20 (95% CI: 2.09, 2.30) for concentration of 110 $\mu\text{g}/\text{m}^3$. Similarly, the visit rate ratios increased as the daily PM_{2.5} concentration increased, but this gradient effect was not significantly higher as the concentration increased. The effect of PM₁₀ was higher on days when the temperature was below the average. Temperature did not affect the association between daily visit counts and PM_{2.5}.

Conclusion: This study found that ambient PM increased the rate of ophthalmology visits due to ocular surface irritation and allergies. Most importantly, this association increased in magnitude with higher ambient PM concentrations. Additional studies are required to fully understand the effects of climate change-related stressors on ocular health.

Plain Language Summary: This study explored the associations between ocular surface irritation and allergy-related daily outpatient office visits with daily ambient particulate matter (PM) levels in the Denver Metropolitan Area. Daily visit counts for ophthalmology outpatient offices were obtained from an academic health center. Daily ambient average concentrations of PM $\leq 10 \mu\text{m}$ in diameter (PM₁₀) and 2.5 micrometers or less in diameter (PM_{2.5}) were obtained. There were 144,313 ocular surface irritation and allergy visits to ophthalmic clinics during the study period. Daily visit counts increased significantly with increasing daily ambient PM₁₀ and PM_{2.5} concentrations, and this association increased in magnitude with higher ambient PM concentrations. Additional studies are required to fully understand the effects of climate change-related stressors on ocular health.

Keywords: particulate matter, ocular surface irritation and allergy

Introduction

Climate change and air pollution have been shown to affect human health and disease through a variety of mechanisms. Importantly, the World Health Organization has declared climate change as “the single biggest health threat to humanity”.¹

The health risks from climate change span a broad range of outcomes, including communicable and non-communicable diseases, extreme weather event-related morbidity and mortality, impact on water and food sources, mental and psychosocial health, and widening of health disparities.^{2–6} The effects of climate and air pollution on chronic diseases such as cardiovascular and renal diseases, lung health, and asthma have been well established.^{7,8} Less studied chronic diseases such as dementia have also been shown to be associated with temperature and air pollutants.^{9–11} Research on the topic of ocular conditions and climate is still in its early stages; therefore, more studies are needed to better understand how climate and air pollutants impact eye health.¹²

Eyes are unique organs that are directly exposed to the environment and are thereby affected by changes in indoor and outdoor elements. The climate can affect the eyes in various ways. In a large survey in the United States, higher temperatures have been associated with higher rates of severe visual impairment.¹³ Ultraviolet exposure caused by ozone depletion can impact eye health. The National Eye Institute estimates that approximately 20% of cataracts are caused by ultraviolet radiation overexposure.¹⁴ Air pollutants such as nitric oxide, sulfur dioxide, and particulate matter (PM) can cause itching, redness, swelling and blurred vision.¹⁵ In addition, temperature, humidity, wind, and dust can contribute to eye irritation.^{16,17} These environmental elements can also disrupt the tear film and lead to chronic ocular surface diseases such as dry eyes.^{18,19}

Three recent reviews of the literature on air pollution and climate for several different types of eye diseases identified scant publications.^{20–22} Another systematic review determined that the eye is the least studied organ with regard to its association with air pollution.²³ Most of the published studies on this topic have determined that climate change adversely affects various ophthalmic conditions, with ocular surface disease (eg, conjunctivitis and dry eye disease (DED)) being both the most studied and the most affected.^{20,22} Ocular surface irritation and conjunctivitis occur when the eyes react to an allergen or similar irritants that cause the eyelids and conjunctiva to become red, swollen, itchy, or dry, and can cause tearing or burning. DED is a common condition that occurs when tears are unable to provide adequate lubrication, leading to inflammation and damage to the eye surface. These ocular conditions often lead to discomfort and potential visual impairment in affected individuals.

The primary purpose of the present study was to assess the associations between the frequency of ocular surface and eye irritation/allergy visits to an academic ophthalmology clinic in the presence of PM in the surrounding community. Specifically, the primary exposures of interest were PM 10 micrometers or less diameter (PM₁₀) and PM 2.5 micrometers or less diameter (PM_{2.5}) pollutants with temperature as a potential effect modifier of this association.

Methods

Study Population and Pollutant Data

This study was deemed exempt by the Colorado Multiple Institutional Review Board and consent from study participants was not required (COMIRB# 23–0143) since data regarding patient visits to ophthalmology did not contain identifying information. The guidelines in the Declaration of Helsinki were followed. In order to explore the relationship between PM and eye health, we examined the frequency of visits to an ophthalmology clinic at the University of Colorado Sue-Anschutz Eye Center. For the analysis involving PM₁₀ we looked at visits by adults over the age of 18 years between October 1st, 2015, and January 27th, 2023. For the analysis involving PM_{2.5}, we looked at adult visits between October 1st, 2015 and December 31st 2020, due to missing PM_{2.5} data. The ophthalmology encounter data were obtained from the billing department of the University of Colorado. Ocular surface irritation and allergy visits were defined as outpatient visits, and the specific International Classification of Disease, 10th revision (ICD-10) codes are listed in Table 1. To correct for individual overutilization of the clinic, any records that represented over three visits per year per individual were removed from the study.

Daily ambient average concentration of PM was obtained from the Environmental Protection Agency (EPA) and included measures for PM₁₀ and PM_{2.5}.²⁴ The EPA aggregates air monitoring data for PM from state, tribal, and other local government agencies. The Colorado Department of Public Health and Environment leads air monitoring in Colorado. Details about monitoring sites, data logging, data quality assurance, and data accessibility can be found in

Table 1 International Classification of Disease (ICD) Codes, Descriptions and Number of Visits During the Study Period

Description	ICD Codes	n
Dry Eye Syndrome	H04.123, H04.122, H04.129, H04.121	67,510
Conjunctivitis	H10.89, H10.33, H10.9, H10.13, H10.409, H10.31, H10.401, H10.45, H10.32, H10.503, H10.023, H10.10, H10.022, H10.30, H10.11, H10.412, H10.239, H10.12, H10.021, H10.413, H10.029, H10.502, H10.403, H10.013, H10.219, H10.012, H10.211, H10.011, H10.423, H10.213, H10.433, H10.421, H10.402, H10.212, H10.232, H10.422, H10.501, H10.523, H10.233, H10.522, H10.411, H10.531, H10.532, H10.533, H10.521, H10.231, H10.429, H10.432, H10.509, H10.419, H10.539, H10.829, H10.823, H10.431, H10.019, H10.821, H10.822	47,093
Ocular Pain	H57.12, H57.11, H57.13	9075
Meibomian gland dysfunction	H02.88A, H02.88B, H02.889	8660
Keratoconjunct sicca	H16.221, H16.223, H16.222	4686
Epiphora	H04.201, H04.203, H04.202	4326
Punctate keratitis	H16.143, H16.142, H16.141	2709
Pingueculitis	H10.813, H10.811, H10.812, H10.819	185
Superficial keratitis	H16.101	53

their technical report.²⁵ Daily maximum temperature and daily average humidity were obtained from Open-Meteo and examined as potential effect modifiers of the primary association.²⁶

Statistical Analysis

Particulate matter and ophthalmology visit data were merged by date. Data were analyzed with distributed lag non-linear models to model the relationship between PM and daily visit counts, while accounting for the cumulative lagged effects of PM₁₀ and PM_{2.5}. Fitting a distributed lag nonlinear model involves the creation of a crossbasis, which is a base that combines initial exposure and lagged exposure. The cross basis can then be used as a predictor in a normal regression model. The cross-basis included a linear structure on the exposure and a polynomial structure on the lags and included a maximum of five lags. The crossbasis was then used in a Poisson generalized linear model. Rate ratios and confidence intervals from the generalized linear model are presented by concentration of PM. PM₁₀ concentrations were 80, 90, 100, and 110 µg/m³ and the PM_{2.5} concentrations were 15, 20, and 25 µg/m³. To explore the potential effect modification of temperature, the data were stratified by being equal to or above the average temperature and below the average temperature.

Results

There were a total of 144,313 ocular surface irritation and allergy visits to the academic ophthalmology clinic during the study period, with an average of 54 visits per day (range, 0–203). The most common ICD code was dry eye syndrome (67,510 visits) followed by conjunctivitis (47,093 visits). All included ICD codes and the number of visits are presented in Table 1. Median daily ambient PM₁₀ and PM_{2.5} concentrations were 24.69 µg/m³ (inter-quartile range (IQR): 16.00, 35.96) and 6.44 µg/m³ (IQR: 4.85, 8.88), respectively.

Daily visit counts increased with increasing daily ambient PM₁₀ and PM_{2.5} concentrations. Five-day cumulative ambient PM₁₀ concentrations at 80, 90, 100, and 110 µg/m³ showed higher rate ratios at each level from 1.77 (95% CI: 1.71, 1.84) at concentration of 80 to 2.20 (95% CI: 2.09, 2.30) for concentration of 110 µg/m³ (Figure 1 and Table 2). Therefore, ophthalmology visits for ocular surface and allergy were 2.2 times higher than the average number of visits when PM₁₀ concentrations were 110 µg/m³, accounting for a five-day lag period. Similarly, the visit rate ratio increased as daily PM_{2.5} concentration increased at each level with 1.10 (95% CI: 1.07, 1.13) at concentration of 15 µg/m³ to 1.17 (95% CI: 1.12, 1.23) at concentration of 25 µg/m³ (Figure 2 and Table 3). Although the rate ratios for each concentration significantly increased for PM_{2.5}, the gradient effect was not significantly higher as the concentration increased for PM_{2.5} as was observed for PM₁₀. The effect of PM₁₀ was greater on days when the temperature was below average than on days

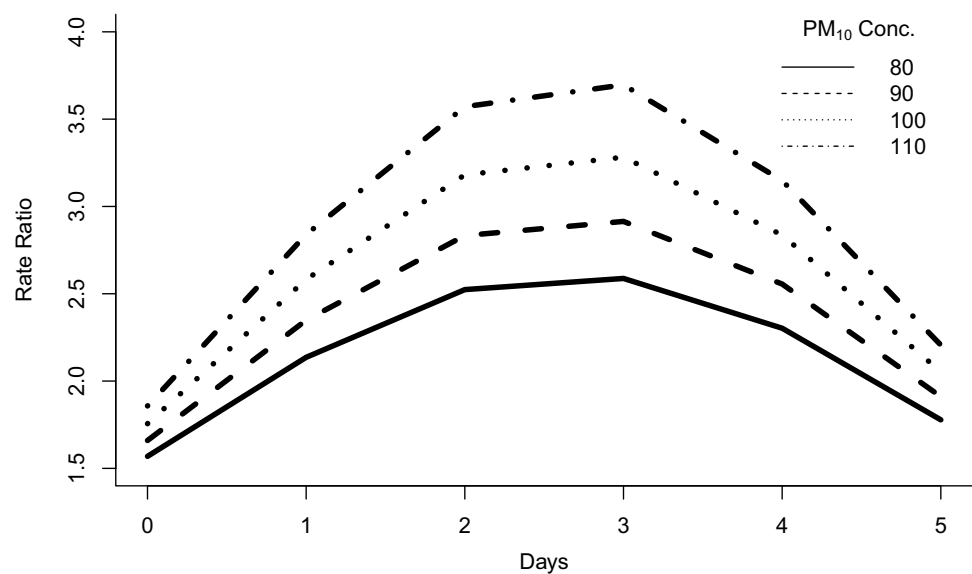


Figure 1 Cumulative effect of PM₁₀ on irritation and allergy ophthalmology visits. The x-axis represents the lag time from particulate matter exposure. The y-axis is the rate ratio of ophthalmology visits. Each line represents various concentrations of PM₁₀ as indicated in the legend.

when the temperature was above average (Table 2). Temperature did not significantly affect the association between PM_{2.5} and the number of visits (Table 3).

Discussion

In this study, we demonstrated that ambient PM concentrations increased the rate of visits to an ophthalmology clinic for ocular surface irritation and allergy in a major metropolitan area in the United States. The magnitude of this association increased significantly as the pollutant concentration for PM₁₀ increased, and the magnitude of the association with PM_{2.5} increased as the concentration increased, but this gradient increase was not significant across concentration levels. When stratified by above- and below-average temperatures, the rate ratios of the number of clinic visits were higher when the temperature was below average for PM₁₀, but not for PM_{2.5}. In addition, these data indicate that health consequences of ocular disease can occur below the Environmental Protection Agency’s established maximum containment levels of 150 µg/m³ for PM₁₀ and 35 µg/m³ for PM_{2.5}.²⁷

Dry eye disease (DED) is one of the most prevalent ophthalmic diseases in the United States and the most common diagnostic code among clinic visits during the study period, accounting for 47% of all visits. DED is a growing public health concern that interferes with quality of life and vision.²⁸ A recently published meta-analysis estimated the prevalence of DED in the United States to be 8.1% (95% CI: 4.9–13.1%), with an incidence among adults of 3.5%.²⁹

Table 2 Rate Ratios of Daily Visits at Lag Day 5 for Daily Average PM₁₀ Concentrations for All Days, Days Below Average Temperature and Days Above Average Temperature

PM ₁₀ Concentration	All Days	Below Average Temperature	Above Average Temperature
	Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)
80	1.773 (1.712, 1.835)	2.630 (2.484, 2.785)	1.672 (1.593, 1.756)
90	1.904 (1.831, 1.980)	2.968 (2.783, 3.166)	1.783 (1.690, 1.884)
100	2.046 (1.959, 2.136)	3.350 (3.118, 3.598)	a
110	2.197 (2.095, 2.305)	3.780 (3.494, 4.090)	a

Notes: ^aThere were no observations in these categories.
Abbreviations: PM, particulate matter; CI, confidence interval.

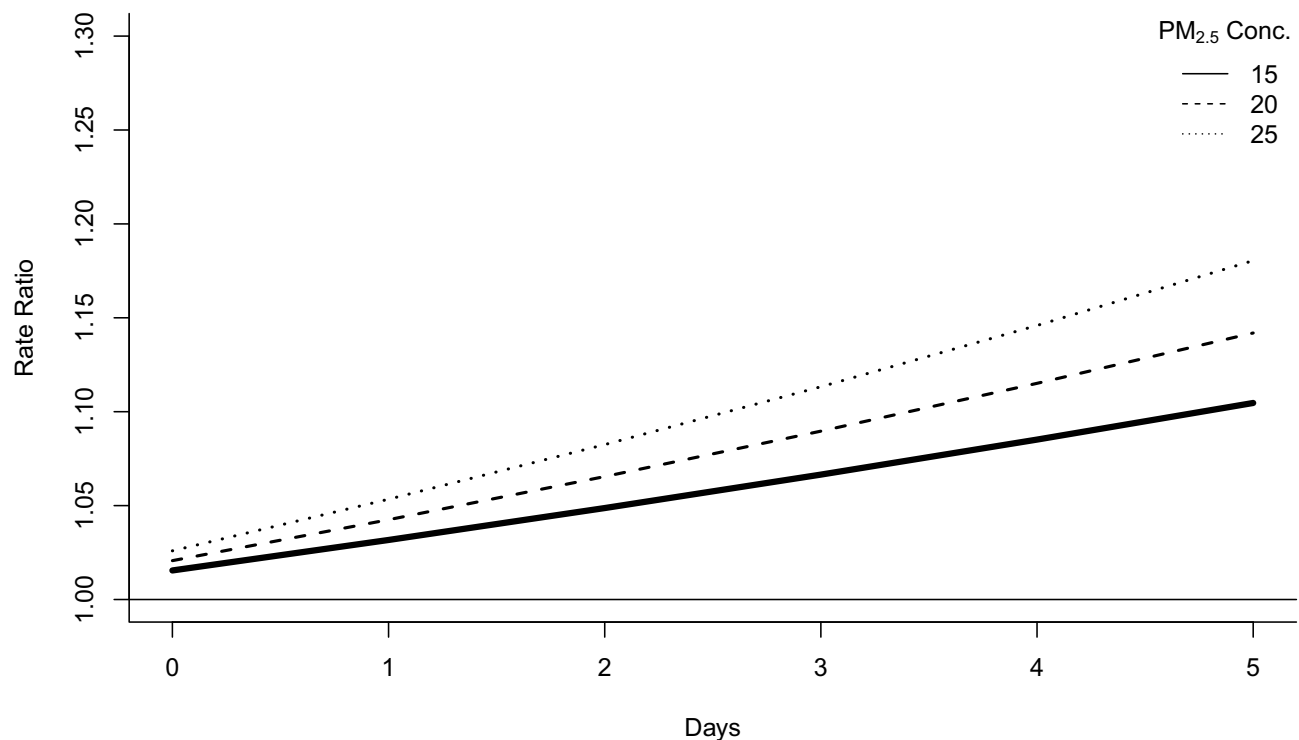


Figure 2 Cumulative effect of PM_{2.5} on irritation and allergy ophthalmology visits. The x-axis represents the lag time from particulate matter exposure. The y-axis is the rate ratio of ophthalmology visits. Each line represents various concentrations of PM_{2.5} as indicated in the legend.

Variation by region and sex has been reported,^{30,31} and prevalence rates may be higher in Colorado due to the dry climate. Similar to our study, two prior studies in China demonstrated associations between adult and pediatric out-patients visits for DED and pollutants PM₁₀ and PM_{2.5}.^{32,33} In contrast, a study in South Korea found no association between PM₁₀ and DED when looking at self-reported DED and annual average of pollutants by region.³⁴ A small study (n=43) of patients with DED found ambient PM₁₀, PM_{2.5} and ozone were correlated with worsening DED clinical measures in South Korea,³⁵ however another study in the United States did not find associations between clinical measures of DED and PM_{2.5}.³¹ A study of self-reported DED among women in Taiwan found higher prevalence rates of DED were associated with PM_{2.5}, and also that DED prevalence rates were associated with higher temperatures and lower humidity, however, after adjustment for individual risk factors of hormone supplements, arthritis and allergy, DED remained associated with higher temperature, but not PM_{2.5}.³⁶

Conjunctivitis was the second most common eye disease among the clinic visits in our study, representing exactly one-third of all the visits. Prevalence rates of ocular allergic conjunctivitis have increased worldwide and vary across regions.³⁷ Socioeconomic and environmental factors such as temperature, humidity, and air pollution have been proposed as contributors to these regional variations.^{37,38} Several previously published studies in Taiwan, Singapore, and China

Table 3 Rate Ratios of Daily Visits at Lag Day 5 for Daily Average PM_{2.5} Concentrations for All Days, Days Below Average Temperature and Days Above Average Temperature

PM _{2.5} Concentration	All Days	Below Average Temperature	Above Average Temperature
	Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)
15	1.100 (1.069, 1.132)	1.068 (1.020, 1.119)	1.142 (1.101, 1.184)
20	1.136 (1.093, 1.180)	1.092 (1.027, 1.161)	1.193 (1.136, 1.253)
25	1.172 (1.118, 1.230)	1.116 (1.034, 1.205)	1.245 (1.173, 1.325)

Abbreviations: PM, particulate matter; CI, confidence interval.

have found that PM₁₀ and PM_{2.5} (but not PM_{2.5} in the Taiwan study) were associated with outpatient visits for nonspecific and acute conjunctivitis.^{39–43} Nucci et al conducted a small study of 132 pediatric visits for conjunctivitis of unknown origin in Milan, Italy, and found that they were associated with PM₁₀ concentrations, but not PM_{2.5}.⁴⁴ Another case-crossover study in Taiwan found that both PM_{2.5} and PM₁₀ were associated with allergic conjunctivitis in univariate, but not multivariable analysis, and a significant association was found between temperature and allergic conjunctivitis in the multivariable model.⁴⁵

Our time-series study has several limitations, including its study design and the inherent weakness of unmeasured confounders, potentially impacting our findings. Clinical visits from only one institution were included in the analyses, and diagnoses for ocular surface irritation and allergy were combined, which are somewhat heterogeneous in their etiologies. One of the strengths of this study is that the time period was over seven years for PM₁₀ analyses and over five years for PM_{2.5}, which allows many days to be included in the model. However, both pollutant analyses included 2020 data, during which clinics operated at low patient volume levels due to the COVID pandemic. This was a short period compared to the entirety of the study and likely had minimal to no impact on the observed associations. Other pollutants such as O₃, NO₂, SO₂, and CO were not available at the same level of granularity and, therefore, not included in the current paper, but are of interest for future research.

The major strength of this study is that we had sufficient variability in PM concentrations to evaluate whether there was a gradient effect of pollutants on patient visits, specifically for PM₁₀. This type of association is important in epidemiological studies and provides evidence supporting an association between PM and ocular diseases. Other strengths of the study include the complex statistical methods incorporating a lag effect of five days, which allows time for patients to seek care for their ocular condition. In addition, stratification by temperature demonstrated the importance of climate factors in the association between air pollution and ophthalmology visits for ocular surface and allergy visits.

Conclusion

Visual health is a significant determinant of quality of life. The effects of climate and air pollution on most ocular diseases have been understudied; however, the importance of visual health is critical to the overall well-being of individuals. The results of this study from one academic clinic demonstrated an association between the air pollutants PM₁₀ and PM_{2.5} on visits specifically for ocular surface irritation and allergy in the Denver Metropolitan Area. This association increased in magnitude with higher ambient PM concentrations. When stratified by above- and below-average temperatures, the rate ratios of the number of clinic visits were higher when the temperature was below average for PM₁₀, but not for PM_{2.5}. Additional research in this field is needed, with the incorporation of more pollutant types, larger population sizes, and broader geographic areas.

Institution Where the Study Was Performed

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Disclosure

The findings of this paper were presented at the 2024 Association for Research and Vision and Ophthalmology (ARVO) conference in Seattle, Washington as a podium presentation in April 2024. The presentation's abstract was published in the ARVO Annual Meeting Abstracts: [Are particulate matter pollutants associated with ophthalmology visits for ocular surface irritation and allergy? | IOVS | ARVO Journals](#).

None of the authors has any proprietary interests or conflicts of interest related to this submission.

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