The Impact of Air Pollution on Disease Activity in Bullous Pemphigoid and Pemphigus

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With a growing awareness of climate change, air pollution has emerged as an important contributor to the development and exacerbation of inflammatory skin conditions. However, the effect of air pollution on immunobullous disease activity is unknown. In this study, we performed a retrospective cohort study of 115 patients with bullous pemphigoid and 152 patients with pemphigus from a university-based specialty clinic in the Southeastern United States. We compared standardized disease activity measures with inhalable particulate matter (particulate matter ≤2.5, particulate matter ≤10), ozone, atmospheric pollutants (sulphur dioxide, carbon monoxide, nitrogen dioxide), and air quality index. Results demonstrated small but statistically significant associations between Bullous Pemphigoid Disease Area Index total activity score and several variables (particulate matter ≤2.5, sulphur dioxide, and air quality index). In addition, there were small but significant negative correlations between ozone and bullous pemphigoid disease area index pruritus score as well as carbon monoxide and pemphigus disease area index score. This study suggests that air pollution may impact disease activity in bullous pemphigoid to a greater extent than pemphigus. Future studies should be aimed at identifying potential mechanisms for this association.

Keywords: Air quality, Climate change, Pemphigoid, Pemphigus, Pollution

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INTRODUCTION

The influence of climate change on health outcomes has become a crucial issue in recent years. Prior studies have demonstrated that air pollution has many wide-ranging health effects, including exacerbation of inflammatory skin diseases such as atopic dermatitis (Nguyen et al, 2019) and acne (Noh et al, 2022) as well as increased risk of skin cancer (Yanagi et al, 2012). Similar observations can be made in autoimmune blistering diseases: small-particle air pollution has been associated with increased risk of hospitalization in pemphigus (Ren et al, 2019), and walnut allergen is implicated in the development of autoantibodies in pemphigus (Lin et al, 2019). However, the effect of air pollution on disease activity in the outpatient setting has not been explored in pemphigus and bullous pemphigoid (BP). To interrogate the effects of air pollution on immunobullous diseases, we conducted a retrospective observational cohort study on patients with established diagnoses of BP and pemphigus at a specialty Autoimmune Blistering Clinic located in an academic center in the Southeastern United States from 2014 to 2020.

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Abbreviations: BP, bullous pemphigoid; PDAI, Pemphigus Disease Area Index; PM, particulate matter; SO2, sulphur dioxide; Th2, T helper 2

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RESULTS

A total of 115 patients with BP (617 unique clinic visits) and 152 patients with pemphigus (1237 clinic visits) were included in the analyses. Air quality index, inhalable particulate matter (PM) with diameter 2.5 mm, and sulphur dioxide (SO_2) were modestly but significantly associated with Bullous Pemphigoid Disease Area Index (PDAI) total activity score (Pearson correlation coefficient = 0.097, 0.097, and 0.083; P = .016, .022, and .041, respectively). Ozone was negatively associated with the Bullous PDAI itch score (Pearson correlation coefficient = −0.095, P = .033). Inhalable PM with diameter ≤10 μm (PM_{10}) or between 2.5 and 10 μm ($PM_{10-2.5}$) were not associated with any clinical variables in BP. Carbon dioxide was modestly negatively associated with PDAI total activity score (Pearson correlation coefficient = −0.059, P = .042) (Table 1).

DISCUSSION

These observations suggest that air pollution may contribute to disease activity in BP to a greater extent than in pemphigus. This corroborates prior findings that high concentrations of particulate matter is associated with disease severity in T helper 2 (Th2)–mediated inflammatory skin diseases, such as atopic dermatitis (Nguyen et al, 2019). BP demonstrates a greater degree of Th2-mediated inflammation compared to pemphigus and therefore may be more responsive to environmental insults. In addition, some patients with pemphigus have mucosal-dominant disease, which may have influenced these findings. Although these correlation coefficients were statistically significant, they were relatively small, suggesting that other factors also play a role in disease activity. One explanation for this is that only ambient

Table 1. Correlation between Air Pollution, BPDAI, and PDAI

	BPDAI Total Activity		BPDAI Pruritus		PDAI	
Environmental Variable	PCC	*P*-value	PCC	*P*-Value	PCC	*P*-Value
Air quality index	0.097	**.016**	−0.017	.698	−0.014	.624
$PM_{2.5}$	0.097	**.022**	0.025	.593	−0.017	.556
PM_{10}	0.055	.183	0.051	.257	−0.037	.194
$PM_{10-2.5}$	−0.018	.676	0.040	.391	−0.031	.295
Ozone	0.015	.716	−0.095	**.033**	−0.023	.421
SO_2	0.083	**.041**	0.016	.711	0.013	.660
CO	0.012	.778	0.000	.999	−0.059	**.042**
NO_2	0.067	.107	−0.001	.981	0.021	.469

Abbreviations: BPDAI, Bullous Pemphigoid Disease Area Index; CO, carbon monoxide; NO_2, nitrogen dioxide; PCC, Pearson correlation coefficient; PDAI, Pemphigus Disease Area Index; PM_{10}, particulate matter with diameter 10 μm; $PM_{10-2.5}$, particulate matter with diameter 2.5−10 μm; $PM_{2.5}$, particulate matter with diameter 2.5 μm; SO_2, sulphur dioxide.

BPDAI was according to Murrell et al (2012), and PDAI was according to Murrell et al (2008). Bold face is used to notate those *P*-values ≤.05.

(outdoor) air pollution was included in this study. However, other sources of air pollution may contribute to disease activity (eg, household air pollution). In addition, there are likely other individual-level and environmental factors that contribute to disease activity.

In this study, SO_2 was positively correlated with disease activity in BP. SO_2 is the most common gaseous sulphur oxide in the environment and primarily results from combustion of sulphur-containing fossil fuels by industrial facilities. Sulphur oxides can also contribute to particulate matter pollution through interactions with other atmospheric compounds. Environmental SO_2 levels have been associated with increased incidence and severity of asthma, likely owing to upregulation of Th2 inflammatory responses through cytokine (IL-4, IL-13) and protein (signal transducer and activator of transcription 6, TRPV1) expression (Li and Yi, 2022; Zhou et al, 2023). BP is a Th2-mediated disease, and it is plausible that SO_2 induces a Th2 proinflammatory response similar to asthma when in contact with epithelial surfaces.

Weaknesses of this study include the retrospective nature and inability to stratify on the basis of covariables such as presence of other allergic-type diseases. However, this relatively large study of 2 rare autoimmune blistering diseases suggests that environmental factors may impact disease activity in BP. Future studies should be aimed at identifying potential mechanisms for this association, determining which environmental factors are the most important, particularly for disease flares, and other factors that contribute to this association.

MATERIALS AND METHODS

Diagnoses of pemphigus and BP were assigned on the basis of typical clinical, histologic, and immunofluorescence findings. Disease activity was measured using the BPDAI (Murrell et al, 2012) and PDAI (Murrell et al, 2008). Flares were defined using standard international consensus definitions (Murrell et al, 2012, 2008). Environmental data, including $PM_{2.5}$, PM_{10}, air quality index, ozone, SO_2, carbon monoxide, and nitrogen dioxide were obtained through the United States Environmental Protection Agency Air Data (https://www.epa.gov/outdoor-air-quality-data). Because $PM_{2.5}$ is included as a component of PM_{10}, $PM_{10-2.5}$ was calculated to investigate PM with a diameter between 2.5 μm and 10 μm. Pearson correlation coefficients were performed in SPSS Statistics (IBM). This study was approved by the Emory Institutional Review Board.

ETHICS STATEMENT

The authors attest that owing to the retrospective nature of this study, it involved no more than minimal risk, and therefore, individual patient consent was not applicable. The study was approved by the Emory University Institutional Review Board.

DATA AVAILABILITY STATEMENT

Datasets related to this article can be obtained upon reasonable request to the corresponding author.

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CONFLICT OF INTEREST

The authors state no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: EFC; Data Curation: EFC, RF; Formal Analysis: EFC; Investigation: EFC, RF; Methodology: EFC, RF; Resources: RF; Software: EFC, RF; Writing - Original Draft Preparation: EFC; Writing - Review and Editing: EFC, RF

DECLARATION OF GENERATIVE ARTIFICIAL INTELLIGENCE (AI) OR LARGE LANGUAGE MODELS (LLMS)

The authors did not use AI/LLM in any part of the research process and/or manuscript preparation.

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