LETTER TO EDITOR

Effects of individual-level exposure of temperature, fine particulate matter, and relative humidity on inhaled corticosteroids use in asthma patients

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To the editor,

Asthma remains a major global health challenge, with symptom severity and control strongly influenced by environmental conditions. Emerging evidence suggested that fluctuations in temperature, increasing levels of fine particulate matter ($PM_{2.5}$), and changes in relative humidity can adversely affect respiratory health and trigger asthma exacerbations. A previous study has shown that exposure to ambient temperature and air pollution was associated with an increased risk of treatment use in asthma (1). However, the association between temperature, $PM_{2.5}$, and relative humidity and the use of inhaled corticosteroids (ICS) has been less thoroughly explored at the individual level. We investigated the association between temperature, $PM_{2.5}$, and relative humidity and the use of inhaled corticosteroids (ICS) in asthma patients. We conducted a retrospective study between January 2008 and December 2021 in asthma patients indicated by ICD-9-CM code 493 and ICD-10-CM code J45, selected from the TMUCRD dataset. Asthma diagnosis was based on the Global Initiative for Asthma (GINA) guideline, which combines medical history, physical examination and supporting examinations (2). This study was approved by the Ethics Committee of the Taipei Medical University-Joint Institutional Review Board. We estimated exposure to temperature, $PM_{2.5}$, and relative humidity using radial basis function interpolation from patient data. The hourly temperature and relative humidity data were obtained from the Central Weather Bureau of Taiwan, and $PM_{2.5}$ were compiled from monitoring stations managed by the Environmental Protection Administration. Following data preprocessing, including organization and quality checks, hourly measurements of temperature, $PM_{2.5}$, and relative humidity were spatially interpolated to each participant's residential location and subsequently averaged to daily values to represent individualized daily exposure. Model performance was refined through cross-validation procedures. Annual average levels of each environmental factor were derived by aggregating the daily data. For each participant, individual exposure histories were then estimated as mean values over 1-day, 7-day, and 30-day periods prior to their recruitment

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date, providing a comprehensive assessment of long-term environmental exposure. Appropriate dosing of ICS is essential for managing patients with persistent or poorly controlled asthma (3). Medium-dose ICS is typically used when low-dose regimens fail to achieve adequate control, providing enhanced anti-inflammatory effects to reduce symptoms and exacerbation risk. For patients with continued disease activity despite medium-dose therapy, escalation to high-dose ICS may be necessary to further suppress airway inflammation. In some cases, high-dose ICS is used in combination with long-acting bronchodilators to optimize therapeutic response and improve lung function in individuals with more severe or refractory asthma. We used the GINA asthma treatment strategy to classify treatment use among patients (4). Treatment was reviewed and adjusted based on the patient's asthma control and response to treatment by the pulmonology specialist. The analysis of the exposure-response relationship was performed using the MGCV package, incorporating age, sex, smoking status, and BMI, as adjusted covariates to understand the association between previous 1-day, 7-day and 30-day of temperature, $PM_{2.5}$, and relative humidity with medium dose ICS-LABA and high dose ICS-LABA use in asthma patients. We included 361,226 asthma patients in this study. The majority of asthma patients were male (58.4%) and the average age was 32.4 years. The average BMI was 58.4 kg/m^2. About 12% of patients was active smoker and 19% was ex-smoker. The average of temperature was 22.6 ± 5.2 °C at 1-day, 22.6 ± 5.0 °C at 7-day and 22.5 ± 4.9 °C at 30-day. In addition, the average concentrations of $PM_{2.5}$ was increased from 18.2 ± 6.8 μg/m^3 at 1-day to 18.3 ± 6.1 μg/m^3 at 5-year and 18.4 ± 6.0 μg/m^3 at 30-day. Moreover, the average relative humidity was 76.2 ± 5.9 % at 1-day, 76.3 ± 5.6 % at 7-day and 76.3 ± 4.8 % at 30-day. The correlations between ambient relative humidity, temperatures and $PM_{2.5}$ in daily mean and difference for 1-day, 7-day, and 30-day averages for study subjects are summarized in Table 1. We observed significant correlation of daily mean exposure for 1-day, 7-day, and 30-day averages for ambient relative humidity, temperatures and $PM_{2.5}$ in asthma patients. In addition, we observed significant correlations of daily difference exposure for 1-day, 7-day, and 30-day averages for ambient relative humidity, temperature, and $PM_{2.5}$ in asthma patients. These relationships likely reflect the interconnected nature of local atmospheric conditions, where shifts in temperature and humidity influence pollutant formation, dispersion, and accumulation. Higher temperatures can enhance secondary aerosol production, while variations in humidity can alter particle size and behavior, contributing to changes in measured $PM_{2.5}$ levels (5). The persistence of these correlations across multiple averaging windows suggests that these environmental factors tend to co-vary over both short-term and longer-term periods, creating combined exposure patterns that may be particularly relevant for asthma outcomes. Simultaneous exposure to changes in temperature, humidity, and $PM_{2.5}$ can collectively exacerbate airway inflammation, impair respiratory defenses, and intensify asthma symptoms more than any single factor alone. We observed an exposure-response relationship for the association of the daily average in the different levels of $PM_{2.5}$ and relative humidity for 1-, 7-, and 30-day periods with medium dose ICS-LABA use in asthma patients (Figure 1). Moreover, we observed an exposure-response relationship for the association of the daily average in the different levels $PM_{2.5}$ and relative humidity for 1-, 7-, and 30-day with high dose ICS-LABA use in asthma patients. Higher or more sustained exposure to particulate pollution and moisture may aggravate airway inflammation, increase bronchial hyperresponsiveness, and weaken mucociliary clearance, thereby prompting the need for intensified controller medication (6). Moreover, a similar pattern was observed for high-dose ICS–LABA use, indicating that as environmental conditions worsen, asthma patients may experience greater symptom burden and instability that require stronger anti-inflammatory and bronchodilatory therapy. Taken together, combined exposure to elevated $PM_{2.5}$ and humidity can amplify respiratory stress, contributing to the escalation of treatment intensity among patients with asthma. This is the first study to investigate the association between environmental exposures and ICS use in asthma patients, particularly focusing on their joint effects. However, several limitations should be acknowledged. First, the analysis did not account for comorbidities

Table 1. Correlation between ambient relative humidity (RH), temperatures and $PM_{2.5}$ in daily mean and difference for 1-day, 7-day, and 30-day averages for study subjects (N = 361226).

	1-day $PM_{2.5}$	7-day $PM_{2.5}$	1-month $PM_{2.5}$	1-day RH	7-day RH	1-month RH	1-day Temperature	7-day Temperature	1-month Temperature
1-day $PM_{2.5}$		0.663**	0.565**	-0.230**	-0.140**	-0.059**	-0.180**	0.255**	-0.295**
7-day $PM_{2.5}$	-0.663**		0.823**	-0.139**	-0.238**	-0.099**	-0.278**	-0.313**	-0.403**
30-day $PM_{2.5}$	0.231**	0.362**		-0.071*	-0.170**	-0.217**	-0.352**	-0.373**	-0.477**
1-day RH	-0.080**	0.029**	0.005		0.114**	-0.132**	-0.311**	-0.350**	-0.438**
7-day RH	-0.140**	-0.238**	-0.114**	0.625**		0.663**	-0.298**	-0.269**	-0.245**
30-day RH	-0.042**	-0.077**	-0.111**	0.220**	0.380**		-0.338**	-0.360**	-0.378**
1-day Temperature	-0.180**	-0.278	-0.311**	-0.204**	-0.298**	-0.338**		0.918**	0.869**
7-day Temperature	-0.082**	0.208**	0.108**	0.014**	-0.128**	0.015**	0.195**		-0.021**
30-day Temperature	-0.012**	0.047**	0.162**	-0.040**	-0.079**	-0.092**	-0.434**	0.431**	

Orange: daily mean; Grey: daily difference. *Abbreviations:* $PM_{2.5}$: particulate matter of <2.5 μm in aerodynamic diameter; RH: relative humidity. $^{*}p < 0.05$; $^{**}p<0.01$.

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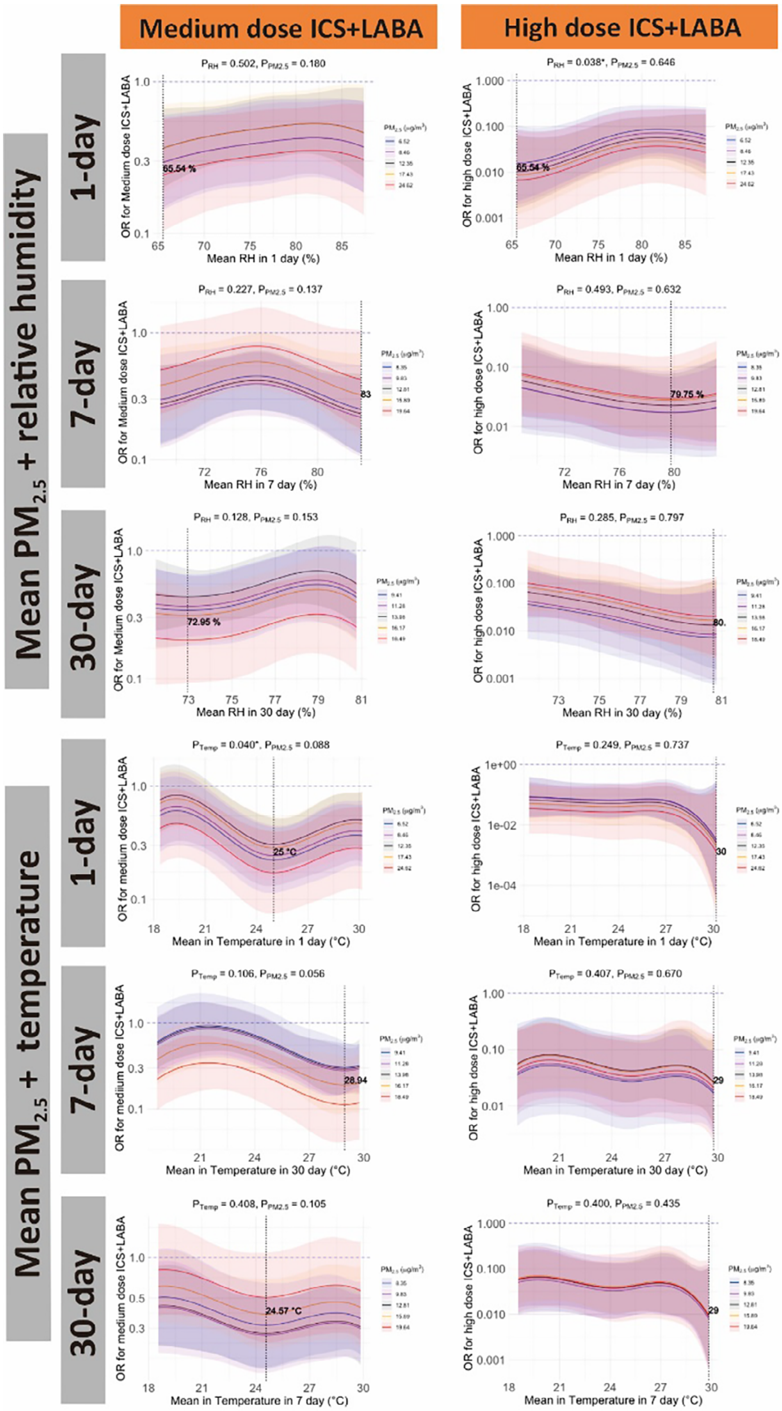

Figure 1. Exposure-response relationship curves for the association of the daily average in the different levels of the particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) and relative humidity (RH) or temperature for 1-, 7-, and 30-day with the step 4 treatments (medium dose ICS-LABA and high dose ICS-LABA). Data are presented as the odds ratio (OR) and 95 % confidence interval (CI). Covariates adjusted for in the models were age, sex, smoking, and the body-mass index (BMI). Asterisk (*) indicates statistical significance at p < 0.05.

such as diabetes, hypertension, and allergic rhinitis, which may influence disease severity and medication requirements. This study also did not account for indoor air pollution which can significantly contribute to overall particulate exposure and may confound the relationship In summary, our findings demonstrate that fluctuations in $PM_{2.5}$, relative humidity, and temperature are significantly associated with increased use of ICS use, particularly high-dose ICS-LABA therapy in asthma patients. Future research should integrate additional clinical factors, indoor air quality metrics, and longitudinal assessments to better clarify the mechanisms underlying these associations and to guide more personalized, exposure-informed asthma management strategies.

Ethic approval: Not applicable.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interests, patent/licensing, arrangement etc-) that might pose a conflict of interest in connection with the submitted article.

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