LETTER TO THE EDITOR

Air pollution and relative humidity increased the risk of multi-drug resistant tuberculosis infections

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To the editor,

Tuberculosis (TB) remains one of the world's leading infectious diseases, driven by airborne transmission and sustained by social and biological vulnerabilities (1). In recent decades, the rise of multi-drug resistant tuberculosis (MDR-TB), which does not respond to at least isoniazid and rifampicin, has intensified global health concerns due to its more complex treatment, higher mortality, and greater potential for community spread. While host- and treatment-related factors are well-established drivers of MDR-TB, growing evidence suggested that environmental conditions also play a significant role in shaping transmission dynamics (2). In particular, air pollution can impair respiratory defenses and increase susceptibility to infection, while relative humidity influences pathogen viability and the behavior of aerosols that carry *Mycobacterium tuberculosis*. Together, these environmental exposures may contribute to a higher risk of MDR-TB, underscoring the need to better understand their impact for more targeted prevention and control strategies. This is a retrospective study between April 2014 and November 2022 in Taipei City of MDR-TB patients. The diagnosis of MDR-TB was confirmed by detecting *Mycobacterium tuberculosis* in culture-positive sputum samples (3). Concentrated acid-fast bacilli (AFB) microscopy and mycobacterial culture were performed on the centrifuged sputum deposits, and the MGIT TBc identification test was used to verify *Mycobacterium tuberculosis* in culture-positive isolates (4). Drug susceptibility testing (DST) was conducted using the Bactec MGIT (Mycobacteria Growth Indicator Tube) system to determine resistance to first-line tuberculosis medications. Patients who were undergoing anticancer treatment or had a confirmed diagnosis of human immunodeficiency virus (HIV) infection were excluded from the study. This study was approved by the Ethics Committee of the Taipei Medical University-Joint Institutional Review Board. We collected the meteorological and particulate matter with an aerodynamic diameter of <2.5μm ($PM_{2.5}$) from the Central Weather Bureau of Taiwan and Environmental Protection Administration. The $PM_{2.5}$, relative humidity (RH), and temperature in hourly-scale was converted into daily scale. The radial basis function (RBF) interpolation methods were used to estimate the daily average values and daily differences value of individual $PM_{2.5}$, RH,

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and temperature. We adjusted for potential confounders using two analytical models. Model 1 included age, sex, body mass index (BMI), and smoking status, while Model 2 further incorporated income as an additional covariate. Prior to analysis, a normality test was conducted to assess whether the data met the assumptions of a normal distribution. We calculated the odds ratio (OR) of outcome variable using logistic regression analysis. We further analyze the exposure-response relationship using MGCV package in R software. All results with *P* value of <0.05 was considered as statistically significant. There were 179 patients with MDR-TB included in this study. The average of age was 57.09 years old with 65.4% of patients was male. The yearly income in this study was 31,813.01 USD per year. About 20.1% of participant was current smoker, whle 21.2% was ex-smoker. We observed that 1-day, 7-day, and 30-day mean of RH was 76.02%, 76.91%, and 76.11%, respectively. In addition, we identified that 1-day, 7-day, and 30-day difference of RH was -0.05%, 0.54%, and 0.17%, respectively. We further observed that average temperature in 1-day, 7-day, and 30-day was 23.73°C, 23.73°C, and 23.79°C, respectively. In addition, we observed that temperature difference in 1-day, 7-day, and 30-day was 0.09°C, 0.11°C, and -0.10°C, respectively. We also observed that $PM_{2.5}$ mean in 1-day, 7-day, and 30-day was 15.07 $\mu g.m^{-3}$, 14.97 $\mu g.m^{-3}$, and 15.44 $\mu g.m^{-3}$, respectively. We identified that $PM_{2.5}$ difference in 1-day, 7-day, and 30-day was -0.35 $\mu g.m^{-3}$, -0.22 $\mu g.m^{-3}$, and -0.13 $\mu g.m^{-3}$, respectively. Associations of the daily mean and difference in the ambient $PM_{2.5}$, RH, and temperature for 1-, 7-, and 30-day mean and MDR-TB infections are summarized in Table 1. We observed that 1% increase in 1-, 7-, and 30-day of RH was associated with an increase in the OR of MDR-TB infection. In addition, we observed that 1°C increase in 1-day and 30-day of temperature was associated with an increase in the OR of MDR-TB infection. In addition, we observed that 1 $\mu g.m^{-3}$ increase in 1-, 7-, and 30-day of $PM_{2.5}$ was associated with an increase in the OR of MDR-TB infection. Our study demonstrated that increases in ambient $PM_{2.5}$, RH, and temperature in 1-, 7-, and 30-day mean were consistently associated with higher odds of MDR-TB infection. A previous study showed

Table 1. Associations of the daily mean and difference in the ambient particulate matter with an aerodynamic diameter of <2.5μm ($PM_{2.5}$), relative humidity (RH), and temperature for 1-, 7-, and 30-day mean and multi-drug resistant tuberculosis infections. Data are presented as the odds ratio (OR) and 95% confident interval (CI).

	OR (95% CI)	**OR (95% CI)**
	Model 1	**Model 2**
RH mean, %		
1-day	**1.023 (1.002-1.044)**	**1.021 (1.002-1.040)**
7-day	**1.055 (1.024-1.086)**	**1.045 (1.022-1.068)**
30-day	**1.073 (1.029-1.118)**	**1.063 (1.025-1.102)**
RH difference, %		
1-day	1.005 (0.979-1.031)	1.007 (0.981-1.035)
7-day	1.004 (0.978-1.030)	0.993 (0.996-1.020)
30-day	1.025 (0.984-1.067)	0.959 (0.920-1.001)
Temperature mean, °C		
1-day	**1.033 (1.001-1.066)**	0.993 (0.961-1.026)
7-day	1.027 (0.991-1.064)	0.994 (0.958-1.030)
30-day	**1.037 (1.001-1.075)**	0.986 (0.950-1.024)
Temperature difference, °C		
1-day	1.032 (0.959-1.112)	0.969 (0.873-1.074)
7-day	1.047 (0.969-1.131)	0.970 (0.896-1.051)
30-day	0.962 (0.902-1.026)	1.039 (0.972-1.111)
$PM_{2.5}$ mean, $\mu g/m^3$		
1-day	**1.036 (1.012-1.060)**	**1.035 (1.014-1.057)**
7-day	**1.046 (1.021-1.071)**	**1.053 (1.023-1.084)**
30-day	**1.051 (1.022-1.080)**	**1.056 (1.020-1.092)**
$PM_{2.5}$ difference, $\mu g/m^3$		
1-day	1.002 (0.982-1.021)	1.000 (0.980-1.021)
7-day	1.006 (0.979-1.034)	1.009 (0.981-1.039)
30-day	0.999 (0.957-1.042)	1.018 (0.975-1.064)

Abbreviations: CI: confidence interval; OR: odds ratio; $PM_{2.5}$: particulate matter with an aerodynamic diameter of <2.5μm; RH: relative humidity. Model 1: Covariates adjusted for age, sex, body mass index (BMI), and smoking status. Model 2: Covariates adjusted for age, sex, body mass index (BMI), smoking status, and income. The bold value indicates statistically significant (p<0.05).

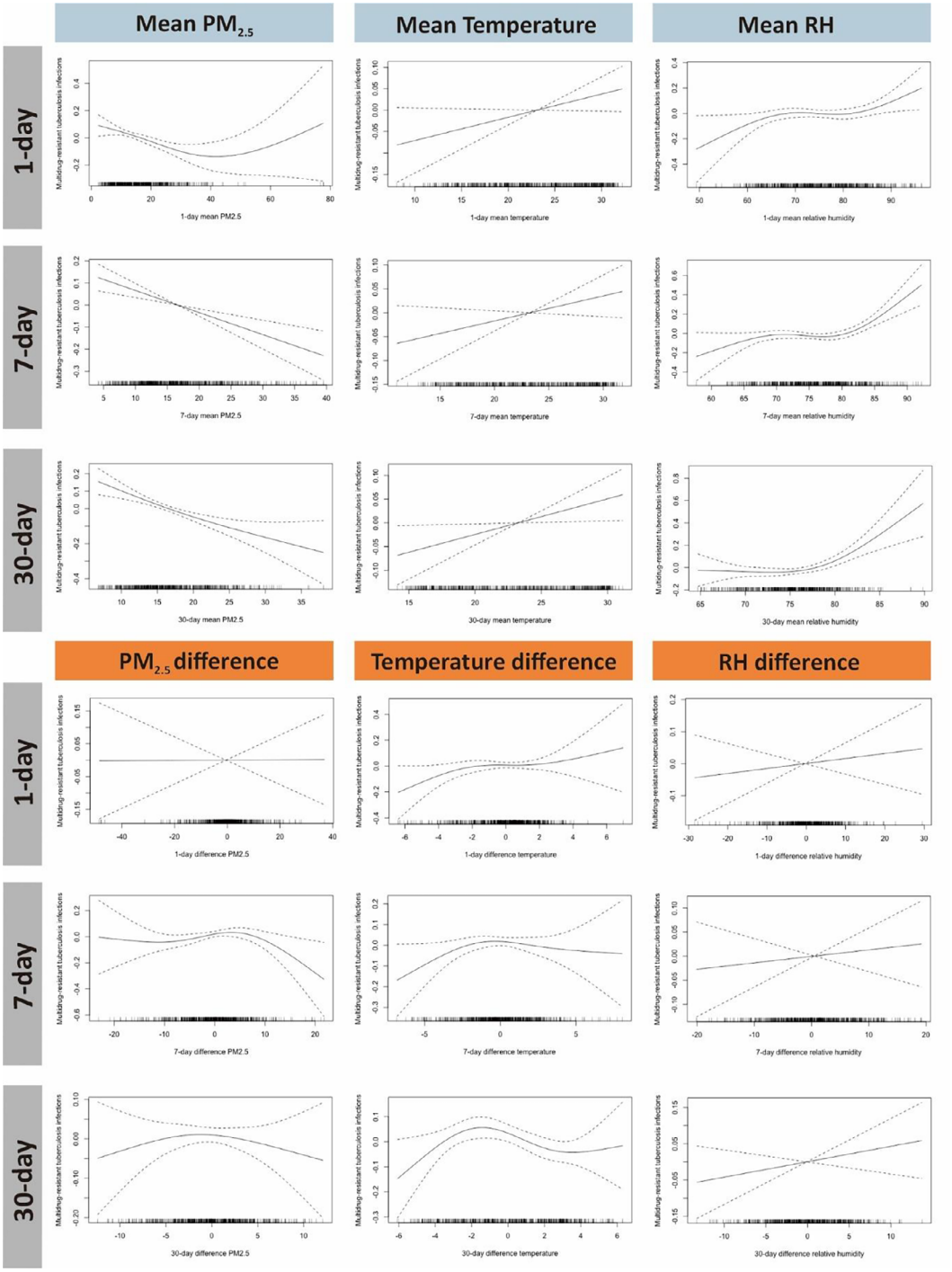

Figure 1. Exposure-response relationship curves for the association of the daily mean and difference in the ambient relative humidity (RH) and temperature or particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) for 1-, 7-, and 30-day mean with the multidrug-resistant tuberculosis infection. Data are presented as the effects and 95 % confident interval (CI). Covariates adjusted in the models were age, sex, body-mass index (BMI), and smoking status.

that high humidity can prolong the survival of *Mycobacterium tuberculosis* in airborne droplets and promote indoor crowding (5). Elevated temperatures have also been linked to increased TB risk, potentially by altering aerosol behavior, influencing indoor congregation during hot conditions, or weakening host immune responses. The positive association between $PM_{2.5}$ and MDR-TB infection aligns with evidence that fine particulate matter impairs pulmonary defenses, induces inflammation, and reduces macrophage function. Together, environmental conditions including air pollution, humidity, and temperature play an important role in increasing the likelihood of MDR-TB infection. Exposure-response relationship for the association of the daily mean and difference in the ambient RH, temperature, and $PM_{2.5}$ for 1-, 7-, and 30-day mean with MDR-TB infection (Figure 1). We observed a non-linear association between ambient mean of $PM_{2.5}$ in 1-day with MDR-TB infection. We also observed a non-linear association between ambient mean of RH for 1-, 7-, and 30-day mean with MDR-TB infection. In addition, we observed a non-linear association between ambient. In addition, we observed a non-linear association between ambient difference of $PM_{2.5}$ for 7-day and 30-day mean with MDR-TB infection. We also observed a non-linear association between ambient temperature difference for 1-, 7-, and 30-day difference with MDR-TB infection. In this study, the exposure–response curves revealed nonlinear associations between ambient RH, temperature, and $PM_{2.5}$ and the risk of MDR-TB. Similar nonlinear patterns have been reported in previous study examining TB and environmental exposures, where both low and high extremes of humidity, temperature, or pollution showed disproportionate effects on transmission and disease progression (6). These non-linear relationships may arise because environmental conditions affect *Mycobacterium tuberculosis* viability, aerosol stability, and host susceptibility in non-uniform ways. Likewise, temperature fluctuations may impair immune responses or alter human behaviors, such as time spent indoors, which modifies exposure opportunities. For $PM_{2.5}$, both acute spikes and prolonged elevated levels can weaken pulmonary defenses, increase airway inflammation, and impair macrophage function, thereby facilitating infection with resistant strains. This study has limitations. Its retrospective design restricts the ability to infer causality, and unmeasured factors, including indoor air pollution, comorbidities, housing ventilation, and detailed socioeconomic conditions may influence results. Although adjustments were made for key demographic and behavioral variables, residual confounding from factors such as occupational exposures, neighborhood environments, and other lifestyle characteristics cannot be ruled out. In conclusion, short- and medium-term exposure to higher levels of ambient $PM_{2.5}$, relative humidity, and temperature is associated with an increased risk of MDR-TB infection.

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.

Authors Contribution: FM, AS, and ANFA contributed substantially to the concept, design, data analyses, interpretation of the data, and completion of the study and manuscript. All authors have read and approved the final manuscript.

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References

1. Gulumbe BH, Abdulrahim A, Ahmad SK, Lawan KA, Danlami MB. WHO report signals tuberculosis resurgence: Addressing systemic failures and revamping control strategies. Decod Inf Trans. 2025;3:100044. doi: 10.1016/j.dcit.2025.100044.
2. Liebenberg D, Gordhan BG, Kana BD. Drug resistant tuberculosis: Implications for transmission, diagnosis, and disease management. Front Cell Infect Microbiol. 2022;12:943545. doi: 10.3389/fcimb.2022.943545.
3. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med. 2007;175(4):367-416. doi: 10.1164/rccm.200604-571ST.

4. Migliori GB, Sotgiu G, Rosales-Klintz S, et al. ERS/ECDC Statement: European Union standards for tuberculosis care, 2017 update. Eur Respir J. 2018;51(5):1702678. doi: 10.1183/13993003.02678-2017.
5. Shadi Y, Morasae EK, Khazaei S, et al. Understanding the mechanisms of climate change impact on tuberculosis: a complex systems approach. BMC Public Health. 2025;25(1):3382. doi: 10.1186/s12889-025-24709-6.
6. Wu Y, Yang J, Wei J, et al. Extreme temperatures amplify air pollution risks to childhood respiratory health in school environment in Jiangsu province, China. Commun Earth Environ. 2025;6(1):429. doi: 10.1038/s43247-025-02409-8.