RESEARCH PAPER

Association of Time-Weighted Air Pollution Exposure with Small Airway functions and Serum Interleukin-6 Levels in Urban Adults

Ananya Dubey[1], Dr. Shobitha Muthukrishnan[2*], Dr. Shilpi Vashishta[3], Dr. Shama Praveen[4], Dr. Manoj Kumar Nandkeoliar[5], Dr. Shalini Rastogi[6]

[1] MD Post graduate student, Department of Physiology, School of Medical Sciences and Research, Sharda University, Greater Noida, U.P.

[2*] Professor, Department of Physiology, School of Medical Sciences and Research, Sharda University, Greater Noida, U.P. (Corresponding Author) - Email: drshobitha@gmail.com

[3] Assistant Professor, Department of Physiology, Government Medical College, Satna, Madhya Pradesh.

[4] Tutor, Dr. Baba Sahib Ambedkar Medical College, New Delhi

[5] Professor Emeritus, Department of Biochemistry, School of Medical Sciences and Research, Sharda University, Greater Noida.

[6] Professor, Department of Physiology, School of Medical Sciences and Research, Sharda University, Greater Noida, U.P.

Affiliation where the work was primarily carried out: Department of Physiology, Sharda School of Medical Sciences and Research, Sharda University, Greater Noida, U.P.

Abstract

Context: Ambient air pollution is a major health concern, with long-term effects well established. Early pathophysiological changes in apparently healthy adults remain underrecognized, and prior studies often overlook individual differences in time spent across polluted microenvironments. Time-weighted exposure models, integrating pollutant concentration with duration of exposure, provide more accurate estimates of personal exposure.

Aim: To examine the relationship between time-weighted air pollution exposure, small airway function, and serum interleukin-6 (IL-6) levels in adults.

Settings and Design: A cross-sectional study was conducted among 126 urban adults.

Methodology: Personal exposure was quantified using the Time-Weighted Exposure Index (TWEI), derived from Air Quality Index values and activity patterns. Small airway function using spirometry and serum IL-6 concentrations using enzyme-linked immunosorbent assay (ELISA) were measured.

Statistical analysis included group comparisons, correlation, and linear regression.

Results: Participants with higher time-weighted exposure demonstrated significantly reduced forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25–75}$%) ($P < 0.05$), while forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) remained preserved. Serum IL-6 levels were significantly elevated in the high-exposure group ($P < 0.05$). A positive correlation was observed between TWEI and IL-6 ($P = 0.032$). Time-weighted exposure independently predicted reduced small airway function and increased IL-6 levels.

Conclusion: Time-weighted air pollution exposure predicts early inflammatory changes, offering a practical tool for detecting risk before disease onset.

Keywords: Air pollution; Time-weighted exposure; Pulmonary function; $FEF_{25–75}$%; Interleukin-6

How to cite this article: Dubey A, Muthukrishnan S, Vashishta S, Praveen S, Nandkeoliar MK, Rastogi S. Association of Time-Weighted Air Pollution Exposure with Small Airway functions and Serum Interleukin-6 Levels in Urban Adults. Int J Drug Deliv Technol. 2026;16(35s): 970-976. DOI: 10.25258/ijddt.16.35s.106

Introduction:

Air pollution is a major environmental health hazard, particularly in the urban areas of low- and middle-income countries where concentrations often exceed recommended limits. [1,2] In India, rapid urbanization, increasing vehicular density, and emissions related to construction have resulted in long-term exposure of large populations to ambient air pollutants. [3] However, while the long-term health effects of this are well recognized, early Patho-Physiological changes in apparently healthy adults are poorly acknowledged. [4]

Fine particulate matter with an aerodynamic diameter ≤2.5 µm ($PM_{2.5}$) has been identified as a principal pollutant responsible for adverse respiratory effects. Owing to its small size, $PM_{2.5}$ can penetrate deep into the distal airways and alveolar regions, where it initiates oxidative stress and inflammatory responses. Repeated exposure to $PM_{2.5}$ has been shown to induce airway inflammation and structural

alterations even in individuals without clinically apparent respiratory disease. [5,6]

Spirometry is conventionally used to assess lung function in clinical and research settings. Dynamic lung parameters, like FEV_1 and FVC, effectively identify established airflow limitation but may fail to detect early airway involvement. [7] In contrast, parameters suggestive of small-airway function, such as $FEF_{25-75}\%$, have been suggested to reflect earlier changes after pollutant exposure. [8,9] Such reductions have been seen in populations with high ambient pollution exposure with preserved FEV_1 values. [9] But the effect of air pollution on combined dynamic lung functions and small airway functions is still not clearly delineated.

In addition to the localized effects on airways, exposure to air pollution is also associated with systemic inflammatory responses. Inhalation of particulate matter can activate immune pathways, resulting in increased production of pro-inflammatory cytokines, including interleukin-6 (IL-6). [10] Such inflammatory responses may play a role in the progression of respiratory dysfunction due to pollution. [11]

Most epidemiological studies evaluate exposure to air pollution based on the air quality index from fixed-site monitoring stations. [12,13] While these metrics are useful for describing population-level exposure, they do not capture individual differences in time spent in various microenvironments. [13] Time-weighted exposure models, which combine pollutant concentration and duration of exposure, may thus more accurately approximate true personal pollution exposure. [14]

To address the limitations of previous studies, the aim of the present study was to evaluate the association between Time-weighted air pollution exposure and Pulmonary function parameters, with particular emphasis on early Small-airway dysfunction, along with serum Interleukin-6 (IL-6) levels among urban adults. The Objectives of this study was to assess pulmonary function parameters in adults with differing levels of time-weighted air pollution exposure and to compare small-airway function indices between low and high exposure groups. Serum IL-6 levels in relation to time-weighted air pollution exposure was evaluated and the relationship between time-weighted exposure scores and Pulmonary function as well as Inflammatory markers were assessed.

Subjects and Methods:

Study design and setting

This cross-sectional observational study was conducted from November,2024 to November,2025 at the Pulmonary Function Lab of a premier medical institute of north India.

Inclusion Criteria

1. Healthy adults aged between 18 and 65 years.
2. Continuous residence in Noida or Greater Noida continuously for at least one year, with variable, but continuously high levels of ambient air pollution in the atmosphere.

Exclusion Criteria

1. History of chronic respiratory diseases like Chronic Obstructive Pulmonary Disease (COPD), Asthma
2. Reported or diagnosed Respiratory infection in the preceding four weeks.
3. Pregnancy.
4. Active smokers

Sample size was estimated based on prevalence estimates from prior studies that reported early physiological alterations associated with the exposure to air pollution. Prevalence estimates ranged from 25-30% in literature. [15] Thus, considering 28% prevalence and a 95% confidence level, and an allowable error of 8%, approximately 121 participants were estimated as the minimum sample size required. Due to some exclusions, a total of 126 participants were included for the final analysis. Assessment of air pollution exposure was assessed using the AQI data obtained from monitoring stations operated by the Central Pollution Control Board (CPCB). [12] AQI values reflect combined concentrations of major pollutants, including PM2.5, PM10, Nitrogen dioxide, Sulfur dioxide, Carbon monoxide, and ozone, and are categorized according to national guidelines.[12] To approximate individual exposure more precisely, a time-weighted air pollution exposure index was calculated for each participant. Written informed consent for participation was obtained. Daily activity pattern information, including time spent indoors and outdoors, while commuting, and at the workplace, was obtained through a structured questionnaire.

For each microenvironment reported, AQI values were multiplied by the respective duration of exposure, and the products summed to yield a Time-Weighted Exposure Index (TWEI), according to environmental exposure assessment methodologies described in the literature .[14]

Time-weighted air pollution exposure index

To estimate individual-level exposure more accurately, a Time-Weighted Exposure Index (TWEI) was calculated by integrating ambient air quality data with self-reported daily activity patterns. [13] For each participant, the number of hours spent in different microenvironments (indoors, outdoors, commuting, and workplace) over a typical day was recorded using a structured questionnaire.

The TWEI was computed using the following formula:

"TWEI"=∑_(i=1)^n⁡〖(AQ〗 I_i×T_i)

Table 1. Structured questionnaire used for assessment of air pollution exposure and daily activity pattern

Section	Variable assessed	Question / item	Response format
Personal information	Age	Age of participant	Years (numeric)
	Gender	Gender	Male / Female / Other
	Occupation	Primary occupation	Open-ended
Daily activity pattern	Predominant environment	Time spent predominantly	Indoors / Outdoors / Both
	Outdoor exposure duration	Average daily time spent outdoors	<1 h / 1–4 h / 4–6 h / 6–8 h / ≥8 h
	Outdoor frequency	Days per week spent outdoors	Days/week
	Type of outdoor activity	Nature of outdoor activities	Walking / Jogging / Cycling / Sports / Commuting / Other
Travel and commuting	Mode of transport	Primary commuting mode	Walking / Bicycle / Personal vehicle / Public transport
	Commute duration	Average daily commute time	Minutes or hours/day
	Traffic exposure	Travel through congested or industrial areas	Yes / No / Sometimes
Residential environment	Proximity to pollution sources	Residence near highways/industrial areas	Yes / No / Not sure
Protective measures	Pollution mitigation	Use of air purifier or filtration at home	Yes / No / Sometimes

where AQI_irepresents the Air Quality Index corresponding to the Ith participant's exposure to air pollution and $T_i$denotes the duration of time (in hours) spent in that microenvironment.

AQI values were categorized according to the national classification system, and weighted scores were assigned based on pollution severity. Increasing weights were applied with higher AQI categories to reflect greater health risk, with lower weights for indoor exposure compared to outdoor exposure. [14] This approach allowed cumulative exposure to reflect both pollutant intensity and duration of contact. The resulting TWEI provided a personalised

estimate of daily pollution burden.

Based on the median Time-Weighted Exposure Index (TWEI) value of 32.8 units, participants were categorised into low-exposure and high-exposure groups. In addition, TWEI was analysed as a continuous variable for correlation analyses.

Pulmonary function assessment

Pulmonary function tests were performed using a computerised portable Spirometer (RMS Helios 702, RMS Instruments, India). [16] At least three acceptable and reproducible maneuvers were obtained for each participant and best values were used for analysis. The following parameters were recorded: FVC, FEV1, FEV1/FVC ratio and FEF25-75%. Predicted values were calculated based on age, gender, and height using the Spirometer software.

Serum IL-6 measurement

Aseptic collection of blood by venipuncture was performed in the morning to minimize diurnal variation. Serum was separated and stored conventionally. Serum IL-6 concentrations were assayed using a commercially available enzyme-linked immunosorbent assay (ELISA) kit. All samples were analysed in batches to reduce inter-assay variability using ELISA 17 kit.

Statistical Analyses: Was performed using SPSS software. Continuous variables are presented as mean ± standard deviation or median with interquartile range, depending on distribution. Comparisons between low and high-exposure groups employed unpaired t-tests or non-parametric equivalents as appropriate. Initial assessment of associations between time-weighted air pollution exposure and physiological parameters utilized correlation analysis. To determine whether exposure independently predicted outcomes, multivariable linear regression analyses were conducted with TWEI as primary predictor, adjusting for age and sex. Separate models were established for small-airway function (FEF25-75%) and serum IL-6 levels. Given

skewness in IL-6 data, a logarithmic transformation was applied prior to regression in order to satisfy normality assumptions. Regression coefficients (β), 95% confidence intervals, and model R^2 values are reported. A *P* -value < 0.05 was considered statistically significant.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of premier medical institute of north India. Ref No. SU/SMS&R/76-A/2024/215.

All procedures were conducted in accordance with ethical standards for human research, and confidentiality of participant data was maintained throughout the study.

Results:

Baseline characteristics of the study population

A total of 126 adults aged between 18 and 65 years of both genders and with a wide range of occupational backgrounds were included in the final analysis. Participants exhibited considerable variability in daily outdoor exposure duration and activity patterns, resulting in a broad distribution of time-weighted air pollution exposure scores in Table 2.

Based on the median Time-Weighted Exposure Index (TWEI) value of 32.8 units, participants were categorized into low-exposure and high-exposure groups. Both groups were comparable with respect to basic demographic characteristics.

Table 2. Baseline Characteristics and Exposure Profile of Participants

Variable	Overall (n = 126)
Age (years), mean ± SD	**39.6 ± 13.8**
Gender (Male/Female), n (%)	**66 (52.4) / 60 (47.6)**
Residence duration ≥1 year, n (%)	**126 (100)**
Daily outdoor exposure (hours), mean ± SD	**5.91 ± 2.67**
Time-Weighted Exposure Index (TWEI), mean ± SD	**64.9 ± 34.0**
Time-Weighted Exposure Index (TWEI), median (IQR)	**51.3 (40.7-85.7)**

Pulmonary function parameters across exposure groups

Participants in the high-exposure group exhibited significantly lower forced expiratory flow between 25% and 75% of vital capacity (FEF_{25-75}%) compared to those in the low-exposure group (*P* < 0.05). P values mentioned in the table. The FEV_1/FVC ratio remained within normal limits across both groups, with no statistically significant difference observed (Table-3)

Serum IL-6 levels and exposure status

Serum interleukin-6 (IL-6) levels were higher among participants in the high-exposure group compared to those in the low-exposure group which was statistically significant (*P* < 0.05). P values are enumerated in the table 3.

Table 3. Comparison of Pulmonary Function Parameters and Serum IL-6 Levels Between Exposure Groups:

Parameters	Low Exposure (n = 75) mean ± SD	High Exposure (n = 51) mean ± SD	*P* -value
FVC (L)	4.13 ± 0.61	1.61 ± 0.53	0.0005
FEV_1 (L)	3.20 ± 0.46	1.27 ± 0.39	0.0003
FEV_1/FVC	0.78 ± 0.04	0.80 ± 0.06	NS
FEF_{25-75} (L/s)	2.69 ± 0.66	1.13 ± 0.61	0.0002
Serum IL-6 (pg/mL), median (IQR)	2.27 (1.50-2.86)	5.72 (4.80-6.17)	0.0007

NS = not statistically significant

Correlation between Time-weighted exposure and Physiological parameters

Correlation analysis demonstrated a significant negative association between TWEI and small-airway function parameters. Higher TWEI values were associated with lower
FEF_{25-75}% values.
In contrast, correlations between TWEI and FEV_1 or FVC were weak and did not reach statistical significance.
A positive correlation was observed between TWEI and serum IL-6 levels, with higher exposure scores associated with higher IL-6 concentrations *(P=0.032*).

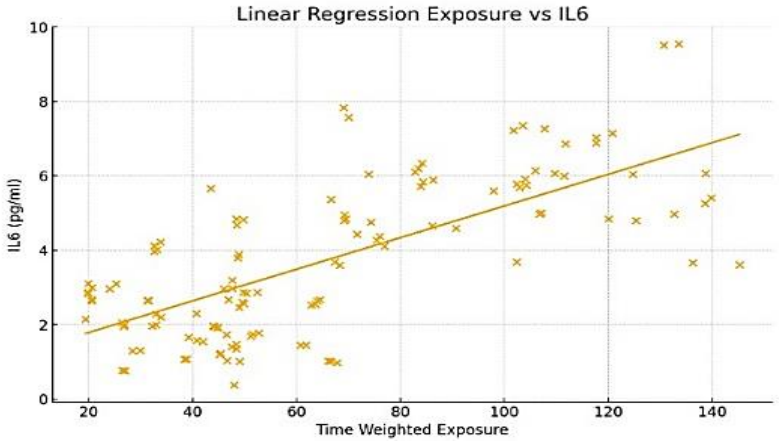

Figure 1: Linear Regression for Air Pollution Expsoure vs IL-6

Multi regression analysis

Table 4. Multivariable Linear Regression Analysis Showing Association of TWEI With Physiological Outcomes

Outcome Variable	β (TWEI)	95% CI	p-value	Model R^2
FEF_{25-75} (L/s)	**−0.0209**	**−0.0243 to −0.0176**	**0.0006**	**0.597**
log(IL-6)	**+0.0117**	**Positive CI**	**0.0009**	**0.402**

Models adjusted for age and gender
IL-6 values were log-transformed due to skewed distribution
β represents change in outcome per unit increase in TWEI

Discussion: The current study explored the relationship between time-weighted exposure to ambient air pollution with small airway functions, dynamic lung function tests and serum levels of Interleukin-6, in a cohort of urban adults. The major findings indicate that high-level time-weighted exposure is associated with early impairment of small-airway functions and increased systemic inflammatory markers, without overt airflow limitation as identified by traditional Spirometric indices.
A striking finding in this study is the preservation of FEV1 and FVC relatively across exposure groups, whereas FEF25-75% was significantly lower among subjects with high exposure scores. This observation agrees with previous findings indicating that small airways are involved early in the process of respiratory injury due to pollution. [17,18] Because the small airways have no cartilaginous support and normally contribute little to total airway resistance, early Pathological alterations could be missed by routine spirometry. [18] This suggests that exclusive reliance on FEV_1 or FEV_1/FVC ratios may underestimate the early Pulmonary effect of air pollution in populations exposed to pollution.The decline in FEF25-75% among the high-exposure group suggests subclinical small-airway dysfunction. Such changes are believed to represent early inflammatory involvement and narrowing of distal airways, which may worsen over time with ongoing exposure. [18] Clinically, these findings highlight the potential utility of including small-airway parameters in routine pulmonary testing, especially in high-risk urban

populations.

Importantly, the association between air pollution exposure and small-airway dysfunction remained after adjustment for age and gender in multivariable regression analyses, indicating that this relationship represents an independent exposure related effect rather than merely demographic variation. A parallel independent association was also observed between time-weighted exposure and serum IL-6 levels, supporting systemic inflammation as a concomitant biological response to chronic pollutant exposure. These findings add to the evidence for a direct exposure response relationship beyond a simple correlation. Beyond pulmonary function alterations, the study observed significantly higher serum IL-6 levels among participants with greater time-weighted pollution exposure. IL-6 is an established marker of systemic inflammation and has been implicated in pollution-related health effects due to its association with immune activation and acute-phase responses . [19]

This interpretation is strengthened by reduced small-airway function and increased IL-6 levels having been simultaneously demonstrated among highly exposed individuals, a suggestion that Pulmonary and Systemic effects of air pollution may occur in tandem. Inhaled particulate matter can cause inflammation in Lungs, leading to spillover of inflammatory mediators into the systemic circulation. Long-term exposure to such mechanisms may promote progressive respiratory impairment and increase susceptibility to cardiopulmonary morbidity. [20]

A key methodological feature of this study was the use of a time-weighted exposure index in order to estimate individual pollution burden. Classic exposure assessment based on ambient air quality index (AQI) values can indeed miss variation in personal exposure due to different daily activities, occupational settings, and commuting patterns.

Because the time-weighted approach combines both pollutant intensity and duration of exposure, it provides a more realistic estimate of environmental burden. Observed associations between the time-weighted exposure index, small-airway function, and Plasma IL-6 levels indicate that this type of personalized exposure metric may improve the detection of exposure-response relationships.

From the standpoint of primary care and public health, these findings have practical implications. Apparently healthy urban adults may still have early patho-physiological and inflammatory changes related to air pollution exposure. This would allow early identification for targeted counseling, monitoring, and preventive interventions among those at increased risk because of prolonged outdoor exposure or occupational vulnerability. History of exposure and selected indices of pulmonary function should be incorporated into routine assessment to assist in recognizing early pollution-related health effects.

Limitations and Future scope of study:

Several limitations need to be acknowledged. The cross-sectional design prohibits causal inference, and longitudinal studies are required to establish temporality between exposure and physiological changes. Exposure assessment was based on ambient AQI data combined with self-reported activity pattern information that may be prone to recall bias and exposure misclassification. Moreover, the study was conducted in one particular urban area that may limit generalizability to other settings with different pollution profiles. Further, number of participant can be increased from the present number to allow for a better representation.

Conclusion:

The present study concludes that, increased time-weighted exposure to ambient air pollution is associated with early impairment of small-airway function and increased serum interleukin-6 levels. Subclinical Pulmonary and inflammatory changes can precede overt airflow limitation and inflammation mediated diseases. The use of an exposure index based on time-weighted averages is representative of individual ambient air pollution exposure in a daily urban environment and underscores the importance of considering environmental exposure history and incorporating sensitive Pulmonary function indices.

Conflict of Interest: None

References:

1. World Health Organization. WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Geneva: World Health Organization; 2021.
2. Health Effects Institute. State of global air 2023. Boston: Health Effects Institute; 2023.
3. Pandey A, Brauer M, Cropper ML, Balakrishnan K, Mathur P, Dey S, et al. Health and economic impact of air pollution in India: evidence from the Global Burden of Disease Study 2019. Lancet Planet Health 2021;5:e25–e38.
4. Schraufnagel DE, Balmes JR, Cowl CT, De Matteis S, Jung SH, Mortimer K, et al. Air pollution and noncommunicable diseases: a review by the Forum of International Respiratory Societies' Environmental Committee. Chest 2019;155:409–416.Li R, Kou X, Geng H, Xie J, Tian J, Cai Z, et al. Effect of ambient PM2.5 exposure on airway inflammation and oxidative stress in adults. Environ Res. 2020;187:109652.

5. Salvi S, Agrawal A. India needs a national strategy to combat air pollution. Lancet Respir Med. 2023;11:451–463.
6. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the Global Lung Function 2012 equations. Eur Respir J. 2012;40:1324–1343.
7. Usmani OS. Small airways disease: a clinical perspective. BMC Pulm Med. 2020;20:178.
8. Tham R, Dharmage SC, Taylor PE, Erbas B, Abramson MJ. Outdoor air pollution and lung function in adults: a systematic review and meta-analysis. Respirology 2019;24:560–568.
9. Rückerl R, Greven S, Ljungman P, Aalto P, Antoniades C, Bellander T, et al. Air pollution and inflammation (IL-6): evidence from controlled exposure and epidemiological studies. Environ Int. 2020;139:105730.
10. Calderón-Garcidueñas L, Villarreal-Calderón R, Valencia-Salazar G, Henríquez-Roldán C, Gutiérrez-Castrellón P, Torres-Jardón R, et al. Systemic inflammation, endothelial dysfunction, and cerebrovascular damage associated with air pollution exposure. Environ Res. 2021;197:111138.
11. Central Pollution Control Board. National Air Quality Index (AQI). New Delhi: Ministry of Environment, Forest and Climate Change, Government of India; 2019.
12. Kaur S, Nieuwenhuijsen MJ, Colvile R. Personal exposure monitoring versus fixed-site monitoring of air pollution:
13. implications for exposure assessment. Environ Int. 2021;147:106317.
14. Jerrett M, Burnett RT, Pope CA, Ito K, Thurston G, Krewski D, et al. Spatial analysis of air pollution and time-
15. activity patterns in exposure misclassification. Environ Health Perspect. 2020;128:067007.
16. Pandey A, Bräuer M, Cropper M, Balakrishnan K, Mathur P, Dey S, et al. Health and economic impact of air pollution in the states of India: the Global Burden of Disease Study 2019. Lancet Planet Health. 2021;5:e25–e38.
17. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26:948–968.
18. Pope CA III, Dockery DW. Health effects of fine particulate air pollution: lines that connect. J Air Waste Manag Assoc. 2006;56:709–742.
19. Bhatt SP, Balte PP, Schwartz JE, Cassano PA, Couper D, Jacobs DR Jr, et al. Discriminative accuracy of $FEF_{25–75}$% for early small airways disease. Am J Respir Crit Care Med. 2021;204:689–700.
20. Hogg JC, Macklem PT, Thurlbeck WM. Site and nature of airway obstruction in chronic obstructive lung disease. N Engl J Med. 1968;278:1355–1360.
21. Rice MB, Ljungman PL, Wilker EH, Gold DR, Schwartz JD, Koutrakis P, et al. Short-term exposure to air pollution and lung function in adults. Am J Respir Crit Care Med. 2013;188:1351–1357

List of Abbreviations:

Abbreviation	Definition
IL-6	Serum interleukin-6
TWEI	Time-Weighted Exposure Index
ELISA	Enzyme -linked immunosorbent assay
FEF25-75%	Forced expiratory flow between 25% and 75% of vital capacity
FVC	Forced vital capacity
FEV1	forced expiratory volume in one second
$PM_{2.5}$	fine particulate matter with an aerodynamic diameter ≤2.5 μm
COPD	Chronic Obstructive Pulmonary Disease
CPCB	The Central Pollution Control Board
AQI	Air quality index

Source(s) of support: Nil

Conflicting Interest (If present, give more details): Nil