A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/JHP1003.

Association of Short-Term Exposure to Air Pollution with Depression in Patients with Asthma: A Cross-Sectional Study in Delhi, India

Vansh Maheshwari,[1] Preeti Negandhi,[1] Vikram Jaggi,[2] Supreet Batra,[3] Poornima Prabhakaran,[4,5] and Jyothi S. Menon[4,5]

[1]Indian Institute of Public Health–Delhi, Public Health Foundation of India, Delhi, India
[2]Asthma Chest & Allergy Centre, Delhi, India
[3]Batra Hospital and Medical Research Centre, Delhi, India
[4]Centre for Health Analytics Research and Trends, Trivedi School of Biosciences, Ashoka University, Haryana, India
[5]Centre for Chronic Disease Control, Delhi, India

Background: Patients with asthma are a population at risk for depression and subsequent mental health risks. Previous studies have suggested that exposure to air pollution is associated with lower asthma control and a higher risk of depression. There is limited evidence on the effect of short-term exposure to air pollution on mental health in susceptible populations, such as patients with asthma.

Objectives: The objective of the present study was to assess the association between short-term exposure (≤30 d) to air pollution and depression in patients with asthma.

Methods: This hospital-based cross-sectional study included 151 consecutively recruited 18- to 65-y-old patients with asthma from two sites in Delhi, India. The Asthma Control Test and the Patient Health Questionnaire-9 were respectively used to assess asthma control and depression status. Data on particulate matter [PM ≤10 and 2.5 μm in aerodynamic diameter (PM_{10} and $PM_{2.5}$, respectively)], nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), and ozone (O_3) were procured from Central Pollution Control Board (CPCB) air quality monitors, and 1-month average exposures were computed using inverse distance weighting (IDW) based on participant residence and workplace address. Ordinal and binary logistic regressions were respectively used to assess the associations for depression status and asthma control with per-unit interquartile range (IQR) increase of air pollution exposure. Sensitivity analyses were conducted using two-pollutant models and mediation effects were evaluated using the Karlson–Holm–Breen method.

Results: Among all participants, 58.3% exhibited depression, and 73.5% had uncontrolled asthma. Adjusted ordinal regression revealed significant associations of PM_{10}, $PM_{2.5}$, NO_2, and SO_2 with increased severity of depression [adjusted odds ratio (aOR) for IQR increase for $PM_{10} = 1.65$ (95% CI: 1.27, 2.16), $PM_{2.5} = 1.65$ (95% CI: 1.22, 2.22), $NO_2 = 2.49$ (95% CI: 1.31, 4.73), and $SO_2 = 1.35$ (95% CI: 1.09, 1.66)]. Similarly, each IQR increase in these pollutants corresponded to significantly lower odds of asthma control [aOR for IQR increase for $PM_{10} = 0.72$ (95% CI: 0.50, 0.98), $PM_{2.5} = 0.68$ (95% CI: 0.47, 0.99), $NO_2 = 0.29$ (95% CI: 0.13, 0.65), and $SO_2 = 0.67$ (95% CI: 0.47, 0.97)]. Asthma control significantly mediated 24.97% and 25.84% of the association of NO_2 and SO_2 exposure, respectively, with depression status. O_3 exposure was not associated with depression status or asthma control.

Conclusions: Our study shows that greater short-term exposure to air pollution may be associated with increased odds of depression and uncontrolled asthma in patients with asthma. Further studies are required to replicate our results and confirm this association. https://doi.org/10.1289/JHP1003

Introduction

Asthma is one of the most common chronic inflammatory diseases of the airways and is characterized by variable respiratory symptoms and episodes of airflow obstruction.[1] In general, asthma is a major concern of public health importance with increasing prevalence rates in many countries. The World Health Organization (WHO) has estimated that asthma affects 262 million people worldwide, of which 30–35 million people are from India.[2] The prevalence of asthma in India is about 2.05%.[3] The symptoms of asthma include cough, chest tightness, fatigue, agitation, chest or abdominal pain, and increased pulse rate. Being a complex disease, asthma can impair the social, physical, and psychological well-being of the affected person.[4]

Depression is one of the most studied mental health disorders, with ∼5% of adults suffering from the disorder globally.[5] Moreover, the prevalence of depression increased by >27% during the coronavirus disease 2019 (COVID-19) pandemic in the years 2020–2021.[6] Patients with asthma have an even higher risk of developing depression, with prevalence of depression ranging from 1% to 45%.[7] There are, however, insufficient studies to determine the prevalence of depression among adult patients with asthma and its impact on the quality of life in such patients in India. Among people with asthma, the majority have reported some restrictions in their life and a poorer health status as compared with individuals without asthma.[8] Such mental health disorders also contribute to poor asthma control,[9] lower treatment adherence,[10] and reduced quality of life.[9,11] Therefore, patients with asthma are a population at risk for depression and subsequent mental health risks. Further, specific symptoms of asthma and depression may coexist,[12] advocating the need to screen patients with asthma for depression and any other psychiatric disorders as a critical component of comprehensive asthma care.

Air pollution is considered to be a major risk factor for asthma and depression. Air pollution includes smoke, gases, and dust particles. Both indoor and outdoor pollution pose a major public health threat as exposure to pollutants such as ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), and particulate matter [PM ≤10 and 2.5 μm in aerodynamic diameter (PM_{10} and $PM_{2.5}$, respectively)], have been found to induce asthma symptoms and exacerbations, to increase hospitalizations, and to decrease lung function in patients with asthma.[13] Mechanistic studies have shown that exposure to air pollution can cause neuroinflammation, oxidative stress in the brain, and cerebrovascular damage, which may lead to the onset of depression.[14] There is evidence that long-term exposure (≥30 d, >6 months) to fine PM ($PM_{2.5}$), NO_2, SO_2, and CO is significantly associated with an augmented risk of depression.[15,16] Even short-term

Address correspondence to Preeti Negandhi, Indian Institute of Public Health–Delhi, Public Health Foundation of India, Delhi, India. Email: preeti.negandhi@iiphd.org

Supplemental Material is available online (https://doi.org/10.1289/JHP1003).
The authors declare they have nothing to disclose.
Conclusions and opinions are those of the individual authors and do not necessarily reflect the policies or views of EHP Publishing or the National Institute of Environmental Health Sciences.
Received 28 September 2023; Revised 14 May 2024; Accepted 14 May 2024; Published 15 August 2024.

exposure (<30 d) to air pollution has been found to be associated with an increased risk of depression.[15] A study conducted by Cho et al. revealed that short-term exposure to air pollutants significantly increased the risk of depressive episodes among individuals with pre-existing asthma.[17]

To the best of our knowledge, there is sparse evidence to corroborate the effect of air pollution on the risk of depression in patients with asthma in India. New Delhi, being one of the most polluted cities in the world,[18] witnesses high levels of PM_{10} and $PM_{2.5}$ every year, especially during the winter season (December to February), mostly attributed to vehicular emission, weather, and stubble burning in neighboring states. This study, therefore, aimed to expand the limited knowledge on the association of air pollution exposure and depression among patients with asthma.

Methods

Study Design, Setting, and Duration

In this cross-sectional study, we recruited patients with asthma from two hospitals (Figure 1A) in Delhi: *a*) the Respiratory Department of Batra Hospital and Medical Research Centre, and *b*) the Asthma Chest & Allergy Centre. These hospitals were selected based on feasibility and sample availability. The study was conducted from January to July 2023.

Study Population

A total of 151 patients with asthma who were between 18 and 65 years of age were consecutively selected and recruited from the outpatient departments of both hospitals. Inclusion criteria considered

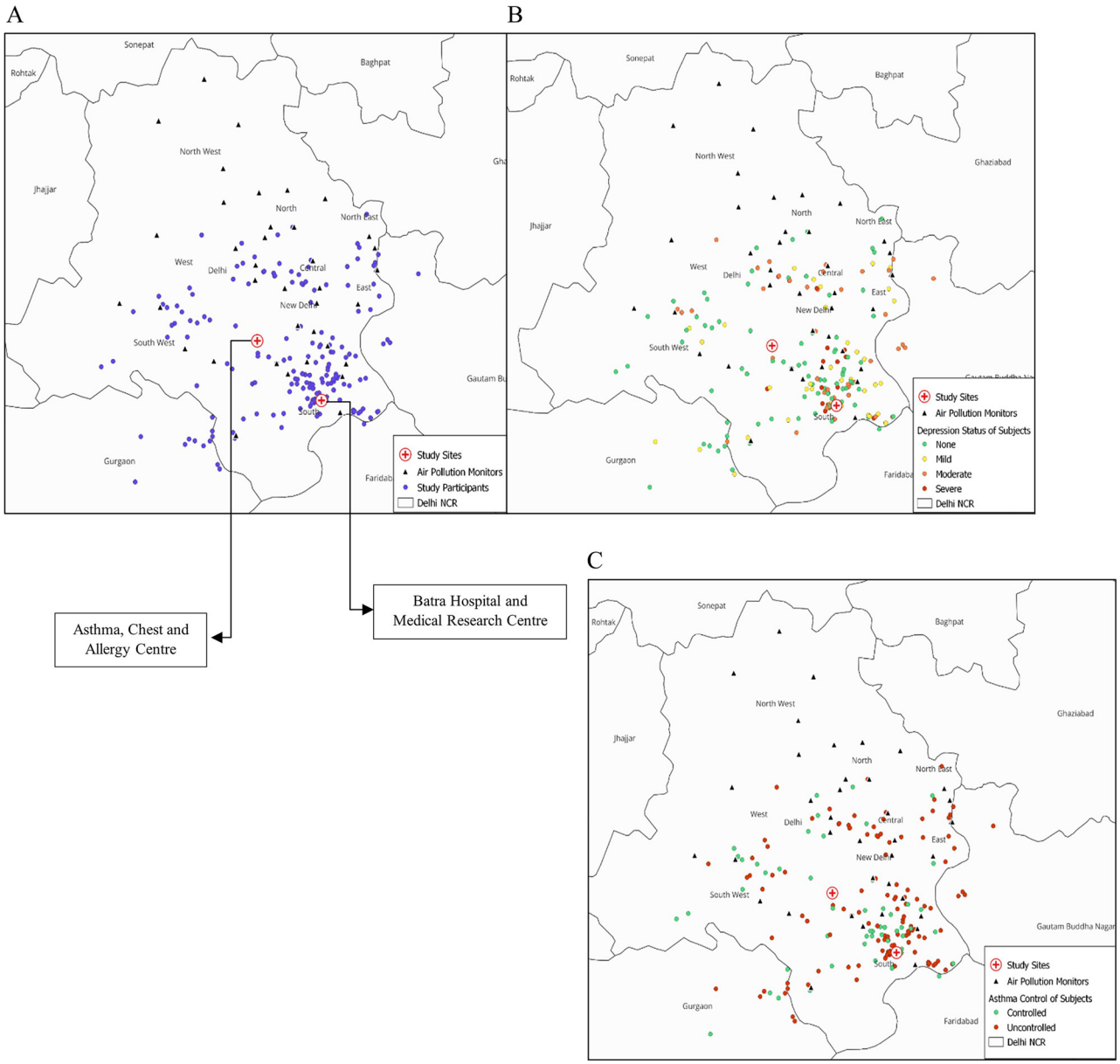

Figure 1. Locations of 151 patients with asthma 18–65 years of age in Delhi: (A) all patients, (B) patients by depression status, and (C) patients by asthma controlled vs. uncontrolled status. Patients with asthma were recruited from two hospitals in Delhi: *a*) the Respiratory Department of Batra Hospital and Medical Research Centre, and *b*) the Asthma Chest & Allergy Centre. The map highlights the locations of these hospitals and participants, providing context for the study's patient population and the regional focus of the research. The maps were made using OSGeo software (version 3.28.2; Open Source Geospatial Foundation). The authors used free shapefiles available at https://projects.datameet.org/maps/states/. Note: NCR, National Capital Region (of Delhi).

for this study were clinical diagnosis of asthma, being between 18 and 65 years of age, and being able to give informed consent. Exclusion criteria were self-reported comorbidities of chest diseases (e.g., pulmonary tuberculosis), pregnant or breastfeeding women, self-reported history of mental health therapy for depression or treatment with antidepressants in the past 3 months, and a travel history outside the National Capital Region (NCR) of Delhi within the past month.

Exposure Assessment

Air pollution data procured from the Central Pollution Control Board (CPCB)[19] air quality monitors were used for the present study. Data are contributed to this network by different central and state agencies, including the CPCB itself, State Pollution Control Boards, the India Meteorological Department, and the Indian Institute of Tropical Meteorology.

The participants' residence and workplace addresses and the location of CPCB monitors were mapped using OSGeo software (version 3.28.2; Open Source Geospatial Foundation). Data for air pollution (PM_{10}, $PM_{2.5}$, NO_2, SO_2, CO, and O_3), averaged over the past month, were used to represent each participant's short-term air pollution exposure. These air pollutant exposures were measured using the inverse distance weighting (IDW) method, which has been widely used to predict target exposure level in the field of environmental exposure assessment.[20] For each patient, we computed predicted air pollution concentrations at their home and workplace address as an IDW average of concentrations at the nearest three monitoring stations,[21] which were selected solely based on proximity, without a predetermined limit for distance or buffer size. The weights were defined as $1/\text{distance}^2$,[22] where distance refers to the distance between the home/workplace address and each neighboring station. For participants who worked, studied, or regularly went to a location within the city other than their home, their exposure per day was assessed using a logical formula: $(\text{hours}_1 \times \text{pollutant}_1 + \text{hours}_2 \times \text{pollutant}_2)/24$ h, where 1 refers to the participant's home and 2 refers to their workplace, educational institute, or other regularly visited place. For 1 and 2, the number of hours were self-reported by the participants and were adjusted based on the number of days per week for the past month.

Other Variables

Information on various covariates and confounders was collected from each participant through an interviewer administered questionnaire. The questionnaire was developed and validated using literature on the effects of lifestyle, family, and society in general, considering the direct and indirect impact these aspects might have on the mental well-being of the individual. Some of the specific covariates considered for this study were age (in years), sex (male or female), per-month total family income (low: <Rs 10,000, moderate: Rs 10,000–Rs 50,000, and high: >Rs 50,000), education level (illiterate/primary, secondary, high school, or college and above), occupation status (not working, homemaker, or currently working), marital status (single, married, or widowed/divorced/separated), smoking status (nonsmoker or former/current smoker), alcohol consumption (no or yes), exercise habit (no, seldom, or usually), sleep difficulties (no or yes), body mass index (BMI; classified as per WHO classification[23] using the measured height and weight of each participant as $<18.5\,\text{kg/m}^2$: underweight, 18.5–24.9 kg/m^2: normal weight, $\geq 25.0\,\text{kg/m}^2$: overweight, and $\geq 30.0\,\text{kg/m}^2$: obese), exposure to dust or smoke for >3 h/d (yes or no), perceived social support (no or yes), living alone (no or yes), number of asthma hospitalizations in the previous year (as per medical records of patient), and whether an air purifier was used (yes or no). The frequency of asthma-related hospitalizations in the previous year (none, ≥1) was reported in the patient's medical records.

Outcomes Assessment

The Patient Health Questionnaire-9 (PHQ-9), a validated tool for psychiatric diagnosis of depression assessment,[24] was used to screen and assess depression status among participants. The PHQ-9 consists of nine questions, each corresponding to one of the nine diagnostic criteria for major depressive disorder listed in the *Diagnostic and Statistical Manual, 4th Edition* (DSM-IV).[25] Each question asks participants to rate how often they felt a depressive symptom in the 2 wk before the assessment. Scores for each item were assigned on a scale of 0 to 3, with a total score ranging from 0 to 27. Severity of depression was based on the scores obtained from the questionnaire, with the cutoff criteria being none (0–4), mild (5–9), moderate (10–14), and moderately severe/severe (≥15) depression.

The Asthma Control Test (ACT), a scientifically tested and commonly used tool for overall self-assessment of asthma control,[26] was used to determine the level of asthma control among the participants, based on the scores obtained from the questionnaire. The ACT comprises five components: *a*) limitations in activity, *b*) shortness of breath, *c*) awakening due to asthma symptoms, *d*) use of reliever medication, and *e*) overall assessment of asthma

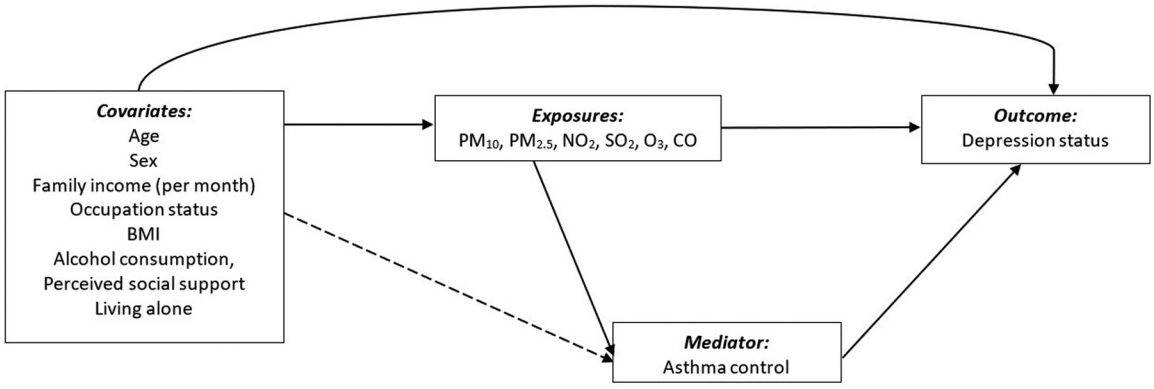

Figure 2. Theoretical model of the mediation of air pollution–depression status association by asthma control (mediator). Conceptual diagram illustrating the mediation analysis using the Karlson–Holm–Breen (KHB) method to explore the relationships between air pollutants (key exposures), asthma control (mediator), and depression status. This theoretical model depicts how asthma control mediates the association between exposure to pollutants and the depression status (none, mild, moderate, and severe) among the study participants. The analysis incorporates ordinal logistic regression to quantify the direct and indirect effects (Table 8). Note: CO, carbon monoxide; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide.

control. Each question is scored on a scale from 1 to 5, with 1 indicating poor control and 5 indicating well-controlled symptoms. The total score ranges from 5 to 25. Controlled asthma was defined with a score of ≥20 points, whereas uncontrolled asthma was categorized as one with a score of <20 points.

Statistical Analysis

The required sample size of 151 was calculated using Open Source for Epidemiological Statistics software (OpenEpi),[27] considering the prevalence of depression in patients with asthma as 11%[28–30] at a significance level of 5%, along with a precision factor of 5%. For the present study, self-reported outcomes of the PHQ-9 (none/mild/moderate/severe) and ACT (controlled/uncontrolled) were treated as categorical variables, and air pollutant exposure as a continuous variable. A descriptive analysis was carried out to understand the characteristics of the study population. Pairwise correlations between air pollutant exposure levels were assessed using Spearman's rank correlation tests. We also conducted a stratified analysis of pollutant exposure data, categorizing by sex and occupation status, to investigate differential impacts across these variables.

Using ordinal logistic regression, each air pollutant exposure was initially incorporated into an individual model as a continuous variable, to calculate odds ratios (ORs) and their 95% confidence intervals (CIs) for the status of depression associated with each increase in the interquartile range (IQR) of exposure. Both crude and adjusted models were constructed for each air pollutant exposure. We performed a variance inflation factor (VIF) analysis on all included variables, removing any variable with a VIF >10 to eliminate significant multicollinearity. Following this, a step-by-step backward elimination of the variables from the model was used to identify those to be retained in the model. Variables were retained in the model if they were associated with depression status at a 5% significance level ($\alpha = 0.05$) or if their inclusion altered existing significant OR estimates by at least 10%. In addition, to assess the nonlinearity of the relationship and illustrate the exposure–response curve between air pollution and depression status, we incorporated the air pollution exposure in the model as a natural cubic spline function. Similar analysis was conducted using a binary logistic regression model to analyze individual associations between each of the air pollutants and the level of asthma control of participants.

To ensure the robustness of our results, sensitivity analyses were performed. Specifically, when a significant relationship was identified between any air pollutant and depression status, two-pollutant models were fitted.[31] This was done to adjust for potential residual confounding effects from other air pollutants.[32–36] In these two-pollutant models, any pair of pollutants exhibiting a correlation coefficient >0.5 were not simultaneously included to avoid the risk of collinearity.

Last, the Karlson–Holm–Breen (KHB) method[37,38] was employed to examine the direct and indirect effects of the pollutants (considered as key exposure) on depression status. We used ordinal logistic regression in our mediation analysis,[39] with asthma control serving as the mediator variable (Figure 2). The total effect of each pollutant was deconstructed in our model into the sum of its direct and indirect effects. The direct effect in this context is the relationship between each pollutant and depression severity, after adjusting for asthma control (mediator) and other covariates. Conversely, the indirect effect pertains to the role of asthma control in mediating the relationship between each pollutant and depression severity. The mediated percentage, calculated as the indirect effect divided by the total effect, represents the proportion of the association attributable to the mediator (asthma control). This percentage was deemed significant only when both the total and indirect effects were statistically significant.

Significance was defined as a $p < 0.05$. There were no missing data in our study. The dataset was complete and all variables of interest were available for every participant. Data analysis was conducted using Stata (version 15.1; StataCorp LLC).

Ethics

Approval to conduct the study was taken from the institutional ethics committee at the Indian Institute of Public Health–Delhi and Scientific Research and the ethical review committee at the Batra Hospital and Medical Research Centre. Formal written approval was given by the medical director of the Asthma Chest & Allergy Centre. A participant information sheet and informed consent form was used to collect prior written consent from the participants. All personal identifiable information (e.g., name, address) was deidentified during analysis and kept confidential. All the procedures established for this study adhered to the Declaration of Helsinki 1964 and were in accordance with the applicable regulatory requirements.

Results

Study Characteristics

A total of 151 patients were included in the present study. Table 1 shows the distribution of participants according to their demographic variables. Approximately 40% ($n = 61$) were older adults (55–65 years of age). Most of the participants were female (57%, $n = 87$) and married (73%, $n = 110$). More than half ($n = 80$) of the participants had a total family income of >Rs 50,000/month.

Table 2 reports the overall lifestyle characteristics of the sample population. More than half of the participants had normal BMI (55.6%), and 11.3% were obese. A majority of the participants did not indulge in smoking (88%) or consumption of alcohol (92%). More than half (63%) of the participants were exposed to dust/smoke on a daily basis for an average of >3 h. Approximately 27% had one or more hospitalizations for asthma in the previous year.

Table 1. Self-reported sociodemographic characteristics of 151 participants with asthma 18–65 years of age in Delhi, India.

Characteristics	*n* (%)
Age group (y)	
Young adults (18–34)	30 (19.87)
Middle-aged adults (35–54)	60 (39.73)
Older adults (55–65)	61 (40.4)
Sex	
Male	64 (42.38)
Female	87 (57.62)
Education	
Primary school or illiterate	20 (13.25)
Secondary	21 (13.9)
High school	41 (27.15)
College and above	69 (45.7)
Marital status	
Single	25 (16.56)
Married	110 (72.84)
Widowed/divorced/separated	16 (10.6)
Total family income (per month)	
<Rs 10,000	18 (11.92)
Rs 10,000–Rs 50,000	53 (35.1)
>Rs 50,000	80 (52.98)
Occupation status	
Working	61 (40.4)
Homemaker	57 (37.75)
Not working	33 (21.85)

Table 2. Self-reported lifestyle characteristics of 151 participants with asthma 18–65 years of age in Delhi, India.

Characteristics	*n* (%)
BMI	
Underweight	9 (5.96)
Normal	84 (55.63)
Overweight	41 (27.15)
Obese	17 (11.26)
Smoking status	
Nonsmoker	133 (88.08)
Former/current smoker	18 (11.92)
Alcohol consumption	
No	139 (92.05)
Yes	12 (7.95)
Exercise habit	
No	51 (33.77)
Seldom	34 (22.52)
Usually	66 (43.71)
Sleep difficulties	
No	93 (61.59)
Yes	58 (38.41)
Exposure to dust/smoke (>3 h/d)	
No	96 (63.58)
Yes	55 (36.42)
Perceived social support	
No	14 (9.27)
Yes	137 (90.73)
Living alone	
No	145 (96.03)
Yes	6 (3.97)
Asthma hospitalizations in previous year	
No	110 (72.85)
≥1 time	41 (27.15)
Serious illness or death in family (in last 6 months)	
No	134 (88.74)
Yes	17 (11.26)
Air purifier usage	
No	115 (76.16)
Yes	36 (23.84)
Asthma control (based on ACT scores)	
Uncontrolled (<20 points)	111 (73.51)
Controlled (≥20 points)	40 (26.49)
Depression status (based on PHQ-9 scores)	
None (0–4)	63 (41.72)
Mild (5–9)	37 (24.5)
Moderate (10–14)	37 (24.5)
Severe (≥15)	14 (9.27)

Note: ACT, Asthma Control Test; BMI, body mass index; PHQ-9, Patient Health Questionnaire-9.

Asthma Control and Depression

With respect to the control of asthma, only 26.5% had well-controlled asthma, based on the scores obtained from the ACT. The mean ± standard deviation (SD) ACT score was 16.11 ± 4.63. Based on PHQ-9 scores, mild-to-severe depression was found in ∼59% of the study participants, and the mean PHQ-9 score among all participants was (7.18 ± 5.45). Figure 1A–C depicts the spread of our study participants across Delhi-NCR and their respective status for depression and asthma control.

Exposure Assessment

One-month average concentrations, and the distribution of air pollution among study participants, are shown in Table 3, and Figure 3 shows the concentrations of air pollutants after IDW across Delhi-NCR for the study participants. Average PM_{10} and $PM_{2.5}$ concentrations after IDW (264.45 $\mu g/m^3$ and 159.53 $\mu g/m^3$, respectively) among the participants were found to be higher than the acceptable standards as per the WHO 2021 Air Quality Guidelines (45 $\mu g/m^3$ and 15 $\mu g/m^3$, respectively).[41] The median

Table 3. Overall descriptive analysis of the air pollution exposure among 151 participants with asthma in Delhi, India.

Pollutants	Mean	SD	Min.	P_{25}	P_{50}	P_{75}	IQR	Max.
PM_{10} ($\mu g/m^3$)	264.45	20.78	202.93	254.56	264.13	271.11	16.55	370.83
$PM_{2.5}$ ($\mu g/m^3$)	159.53	13.71	105.57	153.56	160.76	165.22	11.66	218.25
NO_2 ($\mu g/m^3$)	51.11	13.11	19.94	38.79	53.73	63.06	24.27	80.03
SO_2 ($\mu g/m^3$)	9.23	2.10	4.39	8.14	8.51	9.57	1.43	19.07
O_3 ($\mu g/m^3$)	23.18	3.89	12.09	21.23	23.51	25.20	3.97	39.49
CO (mg/m^3)	1.52	0.27	0.89	1.31	1.58	1.70	0.39	2.41

Note: Recommended levels of air pollutants as per the 2021 World Health Organization Air Quality Guidelines[40] are PM_{10}, 45 $\mu g/m^3$; $PM_{2.5}$, 15 $\mu g/m^3$; NO_2, 25 $\mu g/m^3$; SO_2, 40 $\mu g/m^3$; O_3, 100 $\mu g/m^3$; and CO, 4 mg/m^3. CO, carbon monoxide; IQR, interquartile range; max., maximum; min., minimum; NO_2, nitrogen dioxide; O_3, ozone; P_{25}, 25th percentile; P_{50}, median; P_{75}, 75th percentile; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SD, standard deviation; SO_2, sulfur dioxide.

levels of air pollutants were as follows: median $PM_{10} = 264.13$ (IQR: 254.56–271.11); median $PM_{2.5} = 160.76$ (IQR: 153.56–165.22); median $NO_2 = 53.73$ (IQR: 38.79–63.06); median $SO_2 = 8.51$ (IQR: 8.14–9.57); median $O_3 = 23.51$ (IQR: 21.23–25.20); and median CO = 1.58 (IQR: 1.31–1.70).

The highest concentrations of PM_{10} were observed in East and Central Delhi; $PM_{2.5}$ in Central, East, and South-East Delhi; NO_2 in East and South-East Delhi; SO_2 in East Delhi; O_3 in South and South-East Delhi; and CO in East and South-East Delhi. Table S1 and Figure 4 show the mean air pollution exposure among patients with asthma with respect to different levels of depression. In our analysis, we observed that higher mean concentrations of PM_{10}, $PM_{2.5}$, NO_2, and SO_2 were individually associated with increased reporting of depression levels. Put together, higher depression levels were observed in areas with higher exposures to multiple air pollutants.

As shown in Table 4, the Spearman correlations among air pollutants were generally moderate or low ($r < 0.50$), except for the correlation between PM_{10} and $PM_{2.5}$ ($r = 0.87$), and PM_{10} and O_3 ($r = -0.55$).

Association between Air Pollution and Depression Status

Levels of all air pollutants, except for O_3 and CO, showed a statistically significant association with depression status in the unadjusted analysis (Table 5). Each model was then adjusted for asthma control, age, sex, family income (per month), occupation status, BMI, alcohol consumption, perceived social support, and living alone. Upon adjusted ordinal regression, significantly higher odds of having a greater level of depression severity were observed with each IQR increase in short-term exposure to PM_{10} [adjusted odds ratio (aOR) = 1.65; 95% CI: 1.27, 2.16], $PM_{2.5}$ (aOR = 1.65; 95% CI: 1.22, 2.22), NO_2 (aOR = 2.49; 95% CI: 1.31, 4.73), and SO_2 (aOR = 1.35; 95% CI: 1.09, 1.66). However, an IQR increase in O_3 was associated with lower odds of having a higher depression status (aOR = 0.69; 95% CI: 0.50, 0.96). The ORs and 95% CIs for depression status associated with each 10-$\mu g/m^3$ increase in exposures to PM_{10}, $PM_{2.5}$, SO_2, NO_2, and O_3, as well as a 1-mg/m^3 increase in exposure to CO are summarized in Table S2.

Associations between Air Pollution and Asthma Control

Unadjusted and adjusted associations between air pollution and control of asthma are presented in Table 6. Upon unadjusted analysis, we observed that PM_{10}, $PM_{2.5}$, NO_2, and CO were significantly associated with lower odds of controlled asthma in participants. Upon adjusting for age, sex, family income (per month), smoking status, exercise habit, exposure to dust/smoke, and air purifier usage, it was found that for each IQR increase in short-term exposure to PM_{10} (aOR = 0.72; 95% CI: 0.50, 0.98), $PM_{2.5}$ (aOR = 0.68; 95%

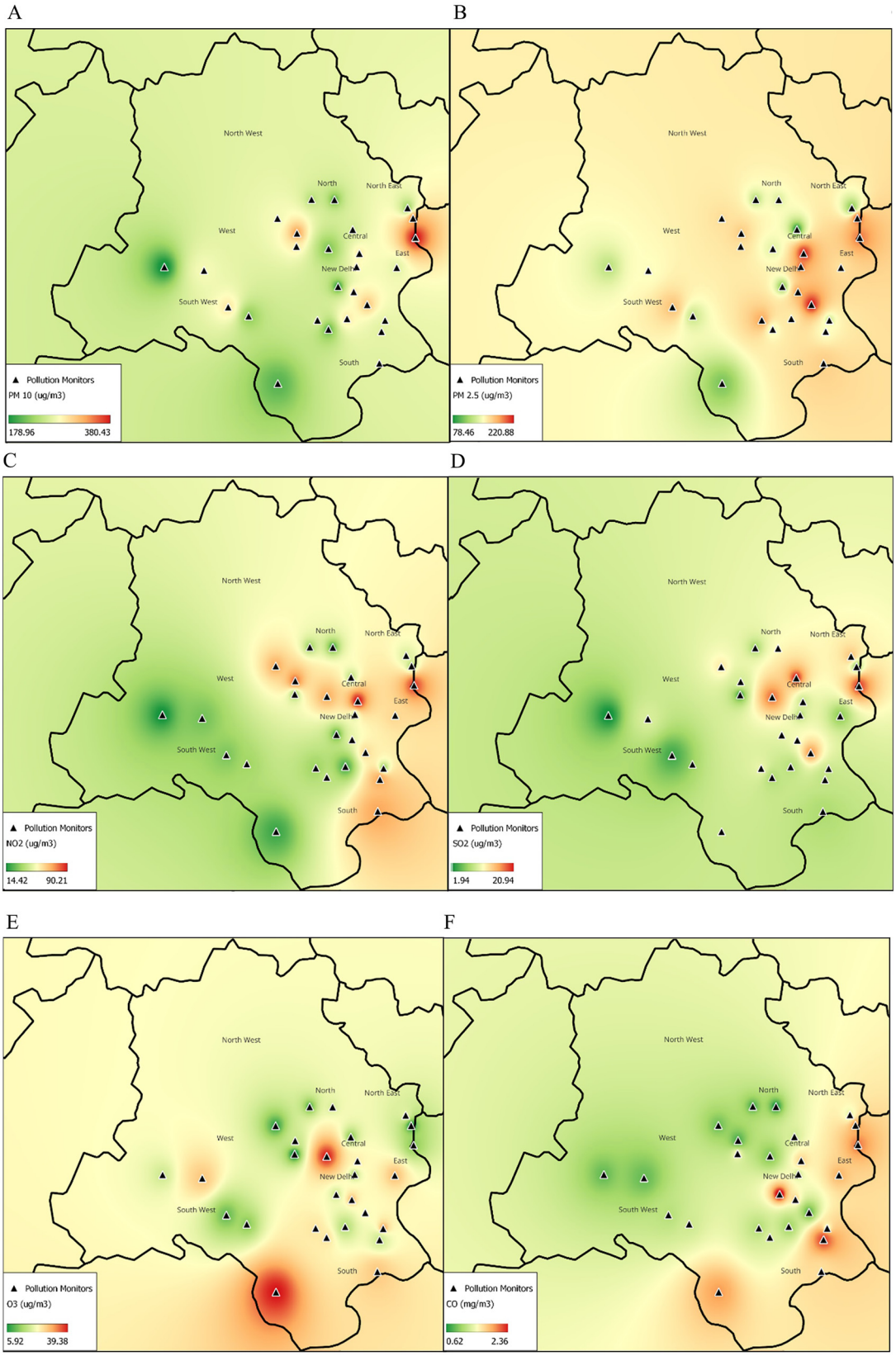

Figure 3. Concentrations of air pollutants across Delhi-NCR as per inverse distance weighting (IDW). This map visualizes the 1-month average concentrations of key pollutants, including (A) PM_{10}, (B) $PM_{2.5}$, (C) NO_2, (D) SO_2, (E) O_3, and (F) CO, among study participants. It highlights regions with the highest concentrations, notably East and Central Delhi for PM_{10}; Central, East, and South-East Delhi for $PM_{2.5}$; and specific areas of heightened NO_2, SO_2, O_3, and CO levels. The maps were made using QGIS software (version 3.28.2; Geospatial Foundation Project). The authors used free shapefiles available at https://projects.datameet.org/maps/states/. Note: CO, carbon monoxide; NCR, National Capital Region (of Delhi); NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with an aerodynamic diameter $\leq$2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter $\leq$10 μm; SO_2, sulfur dioxide.

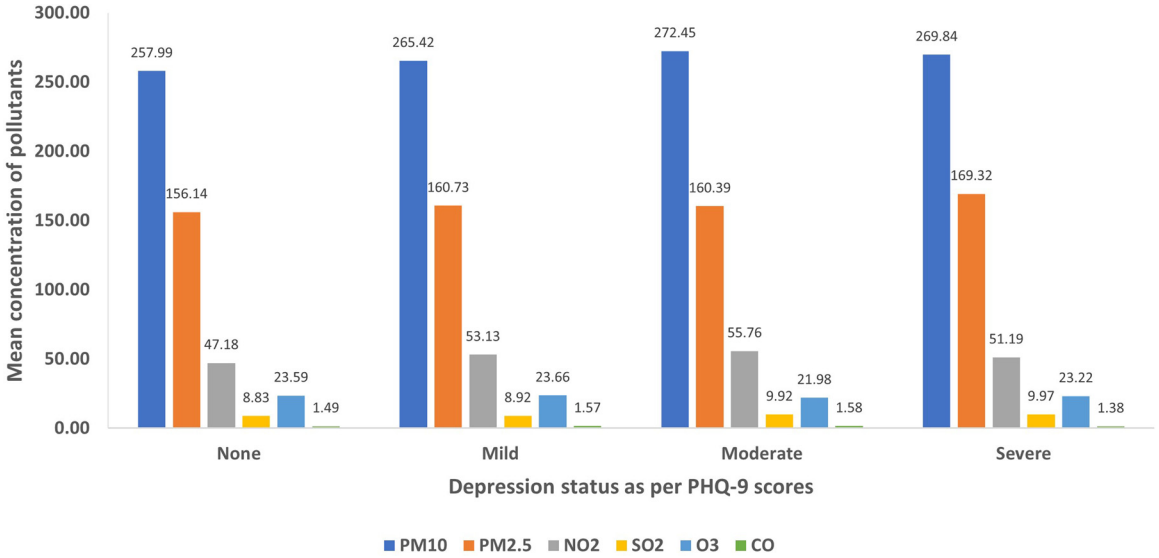

Figure 4. Air pollution exposure and depression status among 151 study participants with asthma in Delhi, India. Graphical representation of the relationship between air pollution exposure and depression status among patients with asthma. The figure displays mean concentrations of PM_{10}, $PM_{2.5}$, NO_2, SO_2, and O_3 (in $\mu g/m^3$), as well as CO (in mg/m^3) from left to right for each category of depression, based on the PHQ-9 score: none (0–4), mild (5–9), moderate (10–14), and moderately severe/severe (≥15) depression (numeric data can be found in Table S1). Note: CO, carbon monoxide; NO_2, nitrogen dioxide; O_3, ozone; PHQ-9, Patient Health Questionnaire-9; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide.

CI: 0.47, 0.99), NO_2 (aOR = 0.29; 95% CI: 0.13, 0.65), and SO_2 (aOR = 0.67; 95% CI: 0.47, 0.97), there was a statistically significant lower odds of having controlled asthma. Each IQR increase in both CO and O_3 showed lower odds of having controlled asthma, but the associations were not statistically significant. Similar associations for asthma control were found for each 10-$\mu g/m^3$ increase of exposures to PM_{10}, $PM_{2.5}$, SO_2, NO_2, and O_3, as well as a 1-mg/m^3 increase of exposure to CO (Table S3).

Two-Pollutant Models

In the sensitivity analysis, the inclusion of other pollutants in the two-pollutant models did not notably alter the associations observed between PM_{10}, $PM_{2.5}$ exposures, and depression status. However, some of the association for SO_2 and NO_2 exposure became insignificant (Table 7).

Mediation of Air Pollution–Depression Association by Asthma Control

Based on the significance of direct and indirect effects, asthma control significantly mediated the association of NO_2 (24.97%) and SO_2 (25.84%) with depression status (Table 8). Higher odds were also observed for the indirect effects for PM_{10} and $PM_{2.5}$; however, these were not statistically significant.

Table 4. Spearman's correlation coefficients between air pollutants.

Pollutants	PM_{10}	$PM_{2.5}$	NO_2	SO_2	O_3	CO
PM_{10}	1.00					
$PM_{2.5}$	0.87*	1.00				
NO_2	0.29*	0.34*	1.00			
SO_2	−0.13	−0.27*	0.11	1.00		
O_3	−0.55*	−0.45*	−0.03	0.27*	1.00	
CO	0.14	0.10	0.40*	−0.25*	0.01	1.00

Note: CO, carbon monoxide; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide. *Pairwise correlation coefficients statistically significant ($p < 0.05$).

Discussion

The study was carried out to assess the association between depression and short-term exposure to air pollution in adult patients with asthma from Delhi. To the best of our knowledge, this is the first hospital-based study in India to address this research objective. Our review of the existing literature incorporates evidence from multiple sources, including human studies, animal models, and *in vitro* experiments. In our sample, more than half of the patients were female, a finding consistent with the evidence that asthma is more prevalent among adult women.[41,42] Our study found a high prevalence of depression (59%), based on PHQ-9 score, in adult patients with asthma who had not been diagnosed with depression. There are limited studies from India that have evaluated the prevalence and risk factors associated with the level of asthma control. Uncontrolled asthma was found in 73.5% of our sample. Similar results were also reported in other hospital-based studies[43,44]

Table 5. Associations between air pollutants and depression status, per IQR increase in exposure to each pollutant among 151 participants with asthma in Delhi, India.

Pollutants	IQR	Unadjusted OR (95% CI)	*p*-Value	Adjusted OR (95% CI)[a]	*p*-Value
PM_{10} ($\mu g/m^3$)	16.55	1.46 (1.16, 1.83)	0.001	1.65 (1.27, 2.16)	<0.001
$PM_{2.5}$ ($\mu g/m^3$)	11.66	1.50 (1.15, 1.97)	0.003	1.65 (1.22, 2.22)	0.001
NO_2 ($\mu g/m^3$)	24.27	2.15 (1.25, 3.72)	0.006	2.49 (1.31, 4.73)	0.005
SO_2 ($\mu g/m^3$)	1.43	1.28 (1.06, 1.54)	0.010	1.35 (1.09, 1.66)	0.006
O_3 ($\mu g/m^3$)	3.97	0.82 (0.62, 1.09)	0.169	0.69 (0.50, 0.96)	0.026
CO (mg/m^3)	0.39	1.08 (0.71, 1.63)	0.731	0.84 (0.52, 1.36)	0.490

Note: Depression status was categorized as none, mild, moderate, or severe based on scores obtained from the Patient Health Questionnaire-9 (PHQ-9) among those not currently diagnosed with depression. ORs were calculated using ordinal logistic regression. An OR >1 indicates that for each unit IQR increase in air pollutant, the odds of being in a more severe category of depression (i.e., moving from none to mild, mild to moderate, or moderate to severe) are greater. Ordinal Hosmer–Lemeshow test for goodness of fit *p*-values are as follows: PM_{10}, 0.62; $PM_{2.5}$, 0.42; NO_2, 0.12; SO_2, 0.17; O_3, 0.37; CO, 0.80. Statistical significance was set at $p < 0.05$. BMI, body mass index; CI, confidence interval; CO, carbon monoxide; IQR, interquartile range; NO_2, nitrogen dioxide; O_3, ozone; OR, odds ratio; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide.
[a]Models were adjusted for asthma control, age, sex, family income (per month), occupation status, BMI, alcohol consumption, perceived social support, and living alone.

Table 6. Associations between air pollutants and asthma control, per IQR increase in exposure to each pollutant among 151 participants with asthma in Delhi, India.

Pollutants	IQR	Unadjusted OR (95% CI)	*p*-Value	Adjusted OR (95% CI)[a]	*p*-Value
PM_{10} ($\mu g/m^3$)	16.55	0.75 (0.54, 0.89)	0.001	0.72 (0.50, 0.98)	0.042
$PM_{2.5}$ ($\mu g/m^3$)	11.66	0.71 (0.51, 0.99)	0.044	0.68 (0.47, 0.99)	0.047
NO_2 ($\mu g/m^3$)	24.27	0.32 (0.16, 0.66)	0.002	0.29 (0.13, 0.65)	0.003
SO_2 ($\mu g/m^3$)	1.43	0.74 (0.53, 1.02)	0.065	0.67 (0.47, 0.97)	0.033
O_3 ($\mu g/m^3$)	3.97	0.96 (0.66, 1.39)	0.819	0.95 (0.63, 1.44)	0.822
CO (mg/m^3)	0.39	0.51 (0.29, 0.88)	0.017	0.56 (0.31, 1.02)	0.057

Note: Asthma control was categorized as uncontrolled or controlled based on scores obtained from the Asthma Control Test. ORs were calculated using binary logistic regression. An OR <1 indicates that for each unit IQR increase in air pollutant, the odds of having controlled asthma decrease. Hosmer–Lemeshow test for goodness of fit *p*-values are as follows: PM_{10}, 0.41; $PM_{2.5}$, 0.37; NO_2, 0.38; SO_2, 0.37; O_3, 0.21; and CO, 0.30. Statistical significance was set at $p < 0.05$. CI, confidence interval; CO, carbon monoxide; IQR, interquartile range; NO_2, nitrogen dioxide; O_3, ozone; OR, odds ratio; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide.
[a]Models were adjusted for age, sex, family income (per month), smoking status, exercise habit, exposure to dust/smoke, and air purifier usage.

conducted in India. Poor asthma control has also been reported among participants in the European Community Respiratory Health Survey II (∼68%).[45] The high rate of uncontrolled asthma is often indicative of nonadherence to medication use,[46] lack of regular follow-up,[47] and inadequate knowledge about self-management of asthma attacks.[48]

Further, our study showed higher short-term exposure to air pollution was associated with greater odds of depression and of having poor asthma control, although not all the associations were statistically significant. It was found that 1-month average exposures to PM_{10}, $PM_{2.5}$, NO_2, and SO_2 were significantly associated with uncontrolled asthma. Previous reports[13,49–51] showed associations of short-term exposures to air pollution with poor control of asthma. Continuous exposure to air pollutants is hypothesized to result in oxidative injury of the airways, leading to reduced lung function and increased asthma attacks.[52] Conversely, the risk of poor asthma control was not significantly associated with O_3 exposure. O_3 is a secondary air pollutant generated from primary air pollutants such as NO_2 via photochemical reaction,[53] so we propose that primary air pollutants might be responsible for triggering uncontrolled asthma before O_3 concentrations begin to increase.

Table 7. Adjusted ORs and 95% CIs of depression status associated with each IQR increase in air pollution exposures using two-pollutant models among 151 participants with asthma in Delhi, India.

Air pollutant	IQR	Model	Adjusted OR (95% CI)[a]	*p*-Value
PM_{10}	16.55	PM_{10}+NO_2	1.53 (1.13, 2.06)	0.005
		PM_{10}+SO_2	1.54 (1.13, 2.10)	0.006
$PM_{2.5}$	11.66	$PM_{2.5}$+NO_2	1.48 (1.06, 2.06)	0.021
		$PM_{2.5}$+SO_2	1.52 (1.12, 2.07)	0.008
NO_2	24.27	NO_2+PM_{10}	1.52 (0.73, 3.13)	0.260
		NO_2+$PM_{2.5}$	1.71 (0.83, 3.50)	0.144
		NO_2+SO_2	2.09 (1.08, 4.06)	0.029
SO_2	1.43	SO_2+PM_{10}	1.11 (0.86, 1.43)	0.408
		SO_2+$PM_{2.5}$	1.25 (0.99, 1.56)	0.054
		SO_2+NO_2	1.26 (1.01, 1.58)	0.039

Note: Depression status was categorized as none, mild, moderate, or severe based on scores obtained from the Patient Health Questionnaire-9 (PHQ-9) among those not currently diagnosed with depression. ORs were calculated using ordinal logistic regression. An OR >1 indicates that for each unit IQR increase in air pollutant, the odds of being in a more severe category of depression (i.e., moving from none to mild, mild to moderate, or moderate to severe) also increase. Ordinal Hosmer–Lemeshow test for goodness of fit for all models was $p > 0.05$. Statistical significance was set at $p < 0.05$. BMI, body mass index; CI, confidence interval; IQR, interquartile range; NO_2, nitrogen dioxide; OR, odds ratio; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide.
[a]Models were adjusted for asthma control, age, sex, family income (per month), occupation status, BMI, alcohol consumption, perceived social support, and living alone.

Similar to our findings, previous studies[15,54] have reported significant associations of short-term exposure to PM_{10}, $PM_{2.5}$, NO_2, and SO_2 with increasing depression levels. One hypothesized mechanism through which exposure to PM (PM_{10} and $PM_{2.5}$) can lead to the manifestation of depression, as evidenced by animal studies, is by inducing oxidative stress and inflammation in the brain.[55] We also found a significant negative association between O_3 exposure and depression status. This may be attributed to the fact that O_3 concentrations are lower in the winter season as compared with spring and summer. Photochemical reactions cause an increase in O_3 concentration[56] during daytime, and therefore, the longer duration of sunlight during summers results in higher O_3 concentrations compared with winters.[57]

Our study highlights the significant associations of SO_2 and NO_2 with asthma control and depression. It has been reported that a healthy person can withstand $\sim 2.62\ \mu g/m^3$ of SO_2 in the ambient air without experiencing any respiratory issues.[58] Delhi has observed a rise in SO_2 and NO_2 concentrations in the more recent years, wherein a notable proportion probably comes from sources that are not local, such as long-distance transportation,[59] thermal power plants fueled by fossil fuels in regions adjacent to Delhi,[60] and burning of biomass in nearby states.[61,62] It is recommended that sustained multisectoral approaches be carefully planned and implemented, to control the rise of air pollutant concentrations, especially for SO_2 and NO_2.

Our results for PM_{10} and $PM_{2.5}$ did not change significantly even after accounting for other pollutants in two-pollutant models. Hence, these findings suggest that each of these air pollutants is at least independently associated with an increased risk of depression. Furthermore, it is noteworthy that asthma control played a significant mediating role in the relationship between NO_2 and SO_2 exposure and the status of depression, accounting for ∼24.97% and 25.84% of their effects, respectively. This highlights the importance of considering asthma control in the context of air pollution and mental health. Some studies have highlighted neuroinflammation as a possible biological mechanism for the effect of air pollutants on mental health.[63–65] However, further studies are necessary to provide biological evidence and describe the causal relationships between air pollution and mental disorders, particularly depression.

This study is novel in that, to our knowledge, it is the first study in India on short-term exposure to air pollution and risk of depression among patients with asthma with comprehensive adjustment of covariates. Short-term exposure to a wider variety of pollutants (PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, and CO) was assessed and compared with previous studies. The air pollution levels were based on data from the CPCB monitors, which provide validated data by national meteorological experts.

Some limitations should be considered when interpreting the present results. First, we did not measure levels of indoor air pollution. Thus, the association between air pollution with asthma control and depression could be underestimated. Future studies may address this limitation by using a personal air pollution monitor. Second, the external validity of the present study is limited given that the study population may not be representative of the general population possibly owing to the nature of the clientele in these hospitals, which includes local residents, referrals, and individuals with chronic cases, thereby leading to selection bias. Similarly, we did not explore depression outcomes in individuals without asthma in Delhi, limiting the study's generalizability beyond the specific asthma population investigated. However, our sample could be considered as representative of patients with asthma with no other major health problems. A final limitation is the cross-sectional design of the study. Longitudinal studies with

Table 8. Mediating effect of asthma control on the association between air pollution exposure and depression status among 151 participants with asthma in Delhi, India.

	Adjusted OR (95% CI)[a]						
Mediator: asthma control	Total effect	*p*-Value	Direct effect	*p*-Value	Indirect effect	*p*-Value	Percentage mediated (%)
PM_{10}	1.83 (1.40, 2.39)	<0.001	1.65 (1.27, 2.16)	<0.001	1.11 (1.00, 1.22)	0.052	16.57
$PM_{2.5}$	1.83 (1.35, 2.47)	<0.001	1.65 (1.22, 2.22)	0.001	1.11 (0.99, 1.24)	0.066	17.40
NO_2	3.38 (1.77, 6.43)	<0.001	2.49 (1.31, 4.73)	0.005	1.36 (1.04, 1.76)	0.023	24.97
SO_2	1.49 (1.20, 1.85)	<0.001	1.34 (1.09, 1.66)	0.006	1.11 (1.02, 1.20)	0.010	25.84
O_3	0.68 (0.49, 0.94)	0.021	0.69 (0.50, 0.96)	0.026	0.99 (0.86, 1.13)	0.839	3.65
CO	1.03 (0.65, 1.65)	0.892	0.84 (0.52, 1.36)	0.490	1.22 (1.01, 1.49)	0.048	6.18

Note: Depression status was categorized as none, mild, moderate, or severe based on scores obtained from the Patient Health Questionnaire-9 (PHQ-9) among those not currently diagnosed with depression. Mediation analysis was conducted using Karlson–Holm–Breen (KHB) method. Direct effect represents the impact of the exposure (air pollutants) on the outcome (depression) directly, that is, not mediated by the mediator (asthma control). Indirect effect quantifies the portion of air pollution exposure's impact on depression that operates through asthma control. Total effect refers to the overall impact of the direct and indirect pathways through which the air pollution exposure influences depression status, encompassing both the direct impact of the pollutants and their effect mediated through asthma control. ORs were calculated using ordinal logistic regression. An OR >1 indicates that for each unit IQR increase in air pollutant, the odds of being in a more severe category of depression (i.e., moving from none to mild, mild to moderate, or moderate to severe) also increase. Statistical significance was set at $p < 0.05$. BMI, body mass index; CI, confidence interval; CO, carbon monoxide; IQR, interquartile range; NO_2, nitrogen dioxide; O_3, ozone; OR, odds ratio; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide.
[a]Models were adjusted for age, sex, family income (per month), occupation status, BMI, alcohol consumption, perceived social support, and living alone.

prospective designs may be conducted in the future to better address the research question.

Conclusion

The present study suggests that greater short-term exposure to PM_{10}, $PM_{2.5}$, NO_2, and SO_2 is associated with increased odds of depression among patients with asthma. Furthermore, PM_{10}, $PM_{2.5}$, NO_2, and SO_2 were negatively associated with control of asthma. Patients with asthma may also have undiagnosed or untreated depression. Therefore, our findings suggest the importance of considering the mental health impacts of air pollution, particularly among patients with asthma. Implementing targeted strategies, such as enhanced screening for depression in this subpopulation, could be crucial in mitigating the mental health consequences of poor air quality.

Acknowledgments

We thank the Central Pollution Control Board (CPCB) for providing the requisite data to support the study. Our sincere gratitude is extended to the two hospitals for their permissions to conduct this work and to the patients with asthma who voluntarily consented to participate in the study.

CPCB data for Delhi and its surroundings can be accessed at https://app.cpcbccr.com/ccr/#/login. Study data can be made available upon suitable request.

References

1. Papi A, Brightling C, Pedersen SE, Reddel HK. 2018. Asthma. Lancet 391(10122):783–800, PMID: 29273246, https://doi.org/10.1016/S0140-6736(17)33311-1.
2. GBD 2019 Diseases and Injuries Collaborators. 2020. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 396(10258):1204–1222, PMID: 33069326, https://doi.org/10.1016/S0140-6736(20)30925-9.
3. Jindal SK, Aggarwal AN, Gupta D, Agarwal R, Kumar R, Kaur T, et al. 2012. Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis in adults (INSEARCH). Int J Tuberc Lung Dis 16(9):1270–1277, PMID: 22871327, https://doi.org/10.5588/ijtld.12.0005.
4. Stanescu S, Kirby SE, Thomas M, Yardley L, Ainsworth B. 2019. A systematic review of psychological, physical health factors, and quality of life in adult asthma. NPJ Prim Care Respir Med 29(1):37, PMID: 31636268, https://doi.org/10.1038/s41533-019-0149-3.
5. WHO (World Health Organization). 2023. Depression. https://www.who.int/health-topics/depression [accessed 12 January 2023].
6. COVID-19 Mental Disorders Collaborators. 2021. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. Lancet 398(10312):1700–1712, PMID: 34634250, https://doi.org/10.1016/S0140-6736(21)02143-7.
7. Opolski M, Wilson I. 2005. Asthma and depression: a pragmatic review of the literature and recommendations for future research. Clin Pract Epidemiol Ment Health 1:18, PMID: 16185365, https://doi.org/10.1186/1745-0179-1-18.
8. Bonala SB, Pina D, Silverman BA, Amara S, Bassett CW, Schneider AT. 2003. Asthma severity, psychiatric morbidity, and quality of life: correlation with inhaled corticosteroid dose. J Asthma 40(6):691–699, PMID: 14580001, https://doi.org/10.1081/JAS-120023491.
9. Lavoie KL, Cartier A, Labrecque M, Bacon SL, Lemière C, Malo JL, et al. 2005. Are psychiatric disorders associated with worse asthma control and quality of life in asthma patients? Respir Med 99(10):1249–1257, PMID: 16140225, https://doi.org/10.1016/j.rmed.2005.03.003.
10. Dong R, Sun S, Sun Y, Wang Y, Zhang X. 2024. The association of depressive symptoms and medication adherence in asthma patients: the mediation effect of medication beliefs. Res Social Adm Pharm 20(3):335–344, PMID: 38110324, https://doi.org/10.1016/j.sapharm.2023.12.002.
11. Bedolla-Barajas M, Morales-Romero J, Fonseca-López JC, Pulido-Guillén NA, Larenas-Linnemann D, Hernández-Colín DD. 2021. Anxiety and depression in adult patients with asthma: the role of asthma control, obesity and allergic sensitization. J Asthma 58(8):1058–1066, PMID: 32312136, https://doi.org/10.1080/02770903.2020.1759087.
12. Mancuso CA, Westermann H, Choi TN, Wenderoth S, Briggs WM, Charlson ME. 2008. Psychological and somatic symptoms in screening for depression in asthma patients. J Asthma 45(3):221–225, PMID: 18415830, https://doi.org/10.1080/02770900701883766.
13. Tiotiu AI, Novakova P, Nedeva D, Chong-Neto HJ, Novakova S, Steiropoulos P, et al. 2020. Impact of air pollution on asthma outcomes. Int J Environ Res Public Health 17(17):6212, PMID: 32867076, https://doi.org/10.3390/ijerph17176212.
14. Babadjouni RM, Hodis DM, Radwanski R, Durazo R, Patel A, Liu Q, et al. 2017. Clinical effects of air pollution on the central nervous system; a review. J Clin Neurosci 43:16–24, PMID: 28528896, https://doi.org/10.1016/j.jocn.2017.04.028.
15. Borroni E, Pesatori AC, Bollati V, Buoli M, Carugno M. 2022. Air pollution exposure and depression: a comprehensive updated systematic review and meta-analysis. Environ Pollut 292(pt A):118245, PMID: 34600062, https://doi.org/10.1016/j.envpol.2021.118245.
16. Braithwaite I, Zhang S, Kirkbride JB, Osborn DPJ, Hayes JF. 2019. Air pollution (particulate matter) exposure and associations with depression, anxiety, bipolar, psychosis and suicide risk: a systematic review and meta-analysis. Environ Health Perspect 127(12):126002, PMID: 31850801, https://doi.org/10.1289/EHP4595.
17. Cho J, Choi YJ, Suh M, Sohn J, Kim H, Cho SK, et al. 2014. Air pollution as a risk factor for depressive episode in patients with cardiovascular disease, diabetes mellitus, or asthma. J Affect Disord 157:45–51, PMID: 24581827, https://doi.org/10.1016/j.jad.2014.01.002.
18. Health Effects Institute. 2022. Comprehensive new report details two major air pollutants and related health impacts in more than 7,000 cities. https://www.healtheffects.org/announcements/comprehensive-new-report-details-two-major-air-pollutants-and-related-health-impacts [accessed 14 August 2023].
19. CPCB (Central Pollution Control Board). 2023. CCR. https://www.cpcb.nic.in [accessed 13 May 2023].
20. Kamboj K, Sisodiya S, Mathur AK, Zare A, Verma P. 2022. Assessment and spatial distribution mapping of criteria pollutants. Water Air Soil Pollut 233(3):82, https://doi.org/10.1007/s11270-022-05522-y.
21. de Mesnard L. 2013. Pollution models and inverse distance weighting: some critical remarks. Comput Geosci 52:459–469, https://doi.org/10.1016/j.cageo.2012.11.002.

22. Shukla K, Kumar P, Mann GS, Khare M. 2020. Mapping spatial distribution of particulate matter using kriging and inverse distance weighting at supersites of megacity Delhi. Sustain Cities Soc 54:101997, https://doi.org/10.1016/j.scs.2019.101997.
23. WHO. 2024. A healthy lifestyle - WHO recommendations. https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle—who-recommendations [accessed 2 January 2024].
24. Kroenke K, Spitzer RL, Williams JB. 2001. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 16(9):606–613, PMID: 11556941, https://doi.org/10.1046/j.1525-1497.2001.016009606.x.
25. American Psychiatric Association. 1994. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Washington, DC: American Psychiatric Publishing.
26. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. 2004. Development of the Asthma Control Test: a survey for assessing asthma control. J Allergy Clin Immunol 113(1):59–65, PMID: 14713908, https://doi.org/10.1016/j.jaci.2003.09.008.
27. Dean AG, Sullivan KM, Soe MM. 2023. Open Source Epidemiologic Statistics for Public Health, Version. https://www.openepi.com/Menu/OE_Menu.htm [accessed 25 February 2023].
28. Sharma BB, Singh S, Sharma VK, Choudhary M, Singh V, Lane S, et al. 2013. Psychiatric morbidity in chronic respiratory disorders in an Indian service using GMHAT/PC. Gen Hosp Psychiatry 35(1):39–44, PMID: 23122486, https://doi.org/10.1016/j.genhosppsych.2012.09.009.
29. Lavoie KL, Bacon SL, Barone S, Cartier A, Ditto B, Labrecque M. 2006. What is worse for asthma control and quality of life: depressive disorders, anxiety disorders, or both? Chest 130(4):1039–1047, PMID: 17035436, https://doi.org/10.1378/chest.130.4.1039.
30. Espinosa Leal FD, Parra Román M, Méndez NHS, Toledo Nicolás DA, Menez Díaz D, Sosa Eroza E, et al. 2006. Anxiety and depression in asthmatic adults in comparison to healthy individuals. Rev Alerg Mex 53(6):201–206, PMID: 17361753.
31. Olmo NRS, do Nascimento Saldiva PH, Braga ALF, Lin CA, de Paula Santos U, Pereira LAA. 2011. A review of low-level air pollution and adverse effects on human health: implications for epidemiological studies and public policy. Clinics (Sao Paulo) 66(4):681–690, PMID: 21655765, https://doi.org/10.1590/S1807-59322011000400025.
32. Finlayson-Pitts BJ Jr, Pitts JN. 1999. *Chemistry of the Upper and Lower Atmosphere: Theory, Experiments, and Applications*. Burlington, MA: Elsevier.
33. Jarvis DJ, Adamkiewicz G, Heroux ME, Rapp R, Kelly FJ. 2010. Nitrogen dioxide. In: *WHO Guidelines for Indoor Air Quality: Selected Pollutants*. https://www.ncbi.nlm.nih.gov/books/NBK138707/ [accessed 31 March 2023].
34. US EPA (US Environmental Protection Agency). 2016. Sulfur Dioxide Basics. https://www.epa.gov/so2-pollution/sulfur-dioxide-basics [accessed 30 March 2023].
35. Hazucha M, Bates DV. 1975. Combined effect of ozone and sulphur dioxide on human pulmonary function. Nature 257:50–51, PMID: 1161004, https://doi.org/10.1038/257050a0.
36. EEA (European Environmental Agency). 2006. Ozone precursor. https://www.eea.europa.eu/help/glossary/eea-glossary/ozone-precursor [accessed 31 March 2023].
37. Karlson KB, Holm A. 2011. Decomposing primary and secondary effects: a new decomposition method. Res Soc Stratif Mobil 29(2):221–237, https://doi.org/10.1016/j.rssm.2010.12.005.
38. Karlson KB, Holm A, Breen R. 2012. Comparing regression coefficients between same-sample nested models using logit and probit: a new method. Sociol Methodol 42(1):286–313, https://doi.org/10.1177/0081175012444861.
39. Smith EK, Lacy MG, Mayer A. 2019. Performance simulations for categorical mediation: analyzing KHB estimates of mediation in ordinal regression models. Stata J 19(4):913–930, https://doi.org/10.1177/1536867X19893638.
40. WHO. 2023. What are the WHO Air quality guidelines? https://www.who.int/news-room/feature-stories/detail/what-are-the-who-air-quality-guidelines [accessed 21 December 2023].
41. Chowdhury NU, Guntur VP, Newcomb DC, Wechsler ME. 2021. Sex and gender in asthma. Eur Respir Rev 30(162):210067, PMID: 34789462, https://doi.org/10.1183/16000617.0067-2021.
42. Singh S, Salvi S, Mangal DK, Singh M, Awasthi S, Mahesh PA, et al. 2022. Prevalence, time trends and treatment practices of asthma in India: the Global Asthma Network study. ERJ Open Res 8(2):00528-2021, PMID: 35651368, https://doi.org/10.1183/23120541.00528-2021.
43. Dua R, Goyal K, Bhatt R, Singh K, Reddy NKK, Sharma P. 2022. An observational study to assess reasons for lack of control among patients of bronchial asthma attending a tertiary care centre in India. Int J Community Med Public Health 9(4):1782–1787, https://doi.org/10.18203/2394-6040.ijcmph20220854.
44. Meena M, Rajawat GS, Arora P, Koolwal S, Sakkarwal HK, Singh AK. 2022. A cross-sectional study to evaluate factors responsible for uncontrolled asthma. Indian J Allergy Asthma Immunol 36(1):34–39, https://doi.org/10.4103/ijaai.ijaai_25_22.
45. Cazzoletti L, Marcon A, Janson C, Corsico A, Jarvis D, Pin I, et al. 2007. Asthma control in Europe: a real-world evaluation based on an international population-based study. J Allergy Clin Immunol 120(6):1360–1367, PMID: 17981317, https://doi.org/10.1016/j.jaci.2007.09.019.
46. Busse WW, Fang J, Marvel J, Tian H, Altman P, Cao H. 2022. Uncontrolled asthma across GINA treatment steps 2−5 in a large US patient cohort. J Asthma 59(5):1051–1062, PMID: 33709871, https://doi.org/10.1080/02770903.2021.1897834.
47. Al-Jahdali H, Ahmed A, Al-Harbi A, Khan M, Baharoon S, Bin Salih S, et al. 2013. Improper inhaler technique is associated with poor asthma control and frequent emergency department visits. Allergy Asthma Clin Immunol 9(1):8, PMID: 23510684, https://doi.org/10.1186/1710-1492-9-8.
48. Al-Jahdali H, Anwar A, Al-Harbi A, Baharoon S, Halwani R, Al Shimemeri A, et al. 2012. Factors associated with patient visits to the emergency department for asthma therapy. BMC Pulm Med 12:80, PMID: 23244616, https://doi.org/10.1186/1471-2466-12-80.
49. Donaldson K, Gilmour MI, MacNee W. 2000. Asthma and PM_{10}. Respir Res 1(1):12–15, PMID: 11667958, https://doi.org/10.1186/rr5.
50. Orellano P, Quaranta N, Reynoso J, Balbi B, Vasquez J. 2017. Effect of outdoor air pollution on asthma exacerbations in children and adults: systematic review and multilevel meta-analysis. PLoS One 12(3):e0174050, PMID: 28319180, https://doi.org/10.1371/journal.pone.0174050.
51. Zheng XY, Orellano P, Lin HL, Jiang M, Guan WJ. 2021. Short-term exposure to ozone, nitrogen dioxide, and sulphur dioxide and emergency department visits and hospital admissions due to asthma: a systematic review and meta-analysis. Environ Int 150:106435, PMID: 33601224, https://doi.org/10.1016/j.envint.2021.106435.
52. Guarnieri M, Balmes JR. 2014. Outdoor air pollution and asthma. Lancet 383(9928):1581–1592, PMID: 24792855, https://doi.org/10.1016/S0140-6736(14)60617-6.
53. Haagen-Smit AJ, Darley EF, Zaitlin M, Hull H, Noble W. 1952. Investigation on injury to plants from air pollution in the Los Angeles area. Plant Physiol 27(1):18–34, PMID: 16654433, https://doi.org/10.1104/pp.27.1.18.
54. Zeng Y, Lin R, Liu L, Liu Y, Li Y. 2019. Ambient air pollution exposure and risk of depression: a systematic review and meta-analysis of observational studies. Psychiatry Res 276:69–78, PMID: 31029037, https://doi.org/10.1016/j.psychres.2019.04.019.
55. MohanKumar SMJ, Campbell A, Block M, Veronesi B. 2008. Particulate matter, oxidative stress and neurotoxicity. Neurotoxicology 29(3):479–488, PMID: 18289684, https://doi.org/10.1016/j.neuro.2007.12.004.
56. Sharma S, Sharma P, Khare M, Kwatra S. 2016. Statistical behavior of ozone in urban environment. Sustain Environ Res 26(3):142–148, https://doi.org/10.1016/j.serj.2016.04.006.
57. Jacob DJ. 2000. Heterogeneous chemistry and tropospheric ozone. Atmos Environ 34(12–14):2131–2159, https://doi.org/10.1016/S1352-2310(99)00462-8.
58. Reno AL, Brooks EG, Ameredes BT. 2015. Mechanisms of heightened airway sensitivity and responses to inhaled SO_2 in asthmatics. Environ Health Insights 9(suppl 1):13–25, PMID: 25922579, https://doi.org/10.4137/EHI.S15671.
59. Mogno C, Palmer PI, Marvin MR, Sharma S, Chen Y, Wild O. 2023. Road transport impact on $PM_{2.5}$ pollution over Delhi during the post-monsoon season. Atmos Environ X 17:100200, https://doi.org/10.1016/j.aeaoa.2022.100200.
60. Saw GK, Dey S, Kaushal H, Lal K. 2021. Tracking NO_2 emission from thermal power plants in North India using TROPOMI data. Atmos Environ 259:118514, https://doi.org/10.1016/j.atmosenv.2021.118514.
61. Dutta A, Jinsart W. 2022. Air pollution in Delhi, India: it's status and association with respiratory diseases. PLoS One 17(9):e0274444, PMID: 36126064, https://doi.org/10.1371/journal.pone.0274444.
62. Nirwan N, Siddiqui A, Kannemadugu HBS, Chauhan P, Singh RP. 2024. Determining hotspots of gaseous criteria air pollutants in Delhi airshed and its association with stubble burning. Sci Rep 14(1):986, PMID: 38200112, https://doi.org/10.1038/s41598-023-51140-x.
63. Block ML, Calderón-Garcidueñas L. 2009. Air pollution: mechanisms of neuroinflammation and CNS disease. Trends Neurosci 32(9):506–516, PMID: 19716187, https://doi.org/10.1016/j.tins.2009.05.009.
64. Armas FV, D'Angiulli A. 2022. Neuroinflammation and neurodegeneration of the central nervous system from air pollutants: a scoping review. Toxics 10(11):666, PMID: 36355957, https://doi.org/10.3390/toxics10110666.
65. Hahad O, Lelieveld J, Birklein F, Lieb K, Daiber A, Münzel T. 2020. Ambient air pollution increases the risk of cerebrovascular and neuropsychiatric disorders through induction of inflammation and oxidative stress. Int J Mol Sci 21(12):4306, PMID: 32560306, https://doi.org/10.3390/ijms21124306.