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ORIGINAL RESEARCH

Frequency of Exacerbations of Chronic Obstructive Pulmonary Disease Associated with the Long-Term Exposure to Air Pollution in the AIREPOC Cohort

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Background: Exacerbations of chronic obstructive pulmonary disease (COPD-E) have been associated with levels of air pollution. The occurrence of COPD-E is associated with increased mortality in this population.

Purpose: To determine the association between long-term exposure to $PM_{2.5}$ and NO_2, and the frequency of COPD-E in patients belonging to AIREPOC, an institutional integrated care program for COPD in Bogota, Colombia.

Patients and Methods: Retrospective cohort study included patients with COPD living in Bogotá, between 2018 and 2021, who received health care in the AIREPOC program. Each patient´s home address was geolocated. Information from local air quality network stations was used to estimate daily and annual mean $PM_{2.5}$ and NO_2 exposure level for each patient using the inverse distance squared weighted regression (IDWR) method. The effect of $PM_{2.5}$ and NO_2 concentrations categorized at 15 $\mu g/m^3$ and 25 $\mu g/m^3$ respectively on the frequency of COPD-E was estimated using a zero-truncated negative binomial model adjusted for potential confounders. Goodness-of-fit was assessed by residuals.

Results: During the observation period, 580 COPD-E occurred in 722 patients. Significant associations were found between COPD-E and NO_2 concentrations $\geq$25 $\mu g/m^3$ (incidence density ratio, RDI: 1.29, 95% CI: 1.02–1.67) after adjustment for sun exposure, COPD severity, depression, and ambient humidity. No association was found between the frequency of COPD-E and $PM_{2.5}$ concentrations $\geq 15 \mu g/m^3$.

Conclusion: Prolonged exposure to high levels of NO_2 increases the frequency of COPD exacerbations in patients residing in Bogotá. These results highlight the importance of strengthening air quality control measures and educating people with COPD to know and interpret the local air quality indices and to follow the recommendations derived from its alterations.

Keywords: air pollution, long-term effect, chronic obstructive pulmonary disease, COPD exacerbations, negative binomial regression truncated at zero

Introduction

Although the adverse effects of air pollution have been widely recognized and air quality programs have been operating in most countries, it remains a major cause of morbidity and mortality.[1] It affects both high-income and low-middle-income countries, where exposure to particulate and gaseous pollutants exceeds the levels recommended by the World Health Organization (WHO).[2,3] According to data from the Global Burden of Diseases, injuries, and Risk Factors (GBD)

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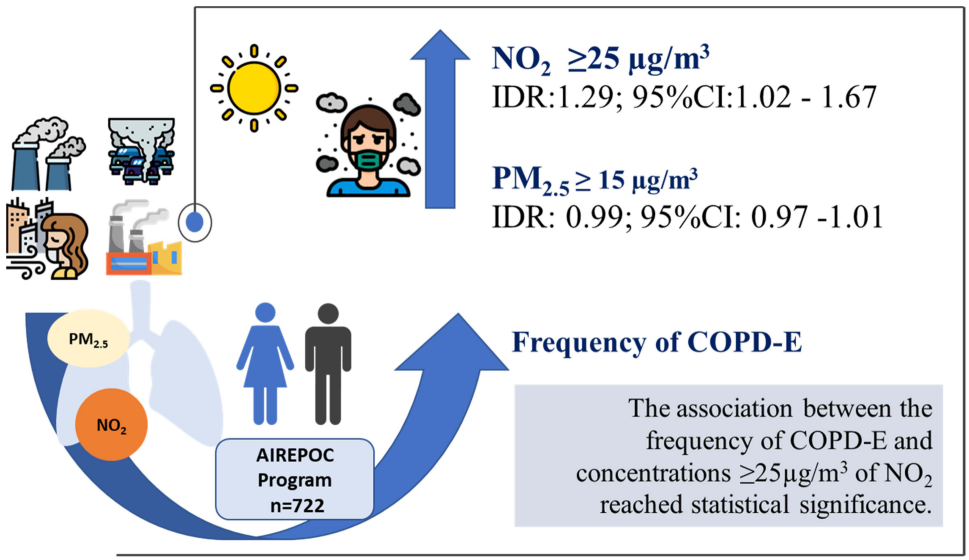
Graphical Abstract



study, air pollution was responsible of 6.67 (95% CI 5.90–7.49) million premature deaths and more than 210 (95% CI 189–240) million disability-adjusted life years (DALYs) in 2019.[4] Air pollution is currently the seventh leading risk factor for non-communicable and communicable diseases,[4] affecting almost all organic systems of the human body (3). About 18% of deaths from exacerbations of chronic pulmonary disease have been attributed to air pollution.[1]

The exacerbations of chronic obstructive pulmonary disease (COPD-E) are considered an important negative event during the disease[5] and have been linked to air pollution.[6–11] COPD-E accelerates lung function decline,[12] reduce quality of life,[13] decrease survival,[5] increase direct costs of care[14–16] and increase the risk of all-cause mortality and acute cardiovascular events.[17–20] Moderate to severe exacerbations increase the risk of future exacerbations and the risk of death.[21] A history of exacerbations is the most important predictor of future exacerbations.[17,21] Therefore, identifying patients at risk for COPD-E is important to reduce the burden of the disease and prevent the cycle of lung damage, worsening quality of life, increased disease burden, increased healthcare costs, and death.[21]

The long-term exposure to air pollution has been associated with the development of COPD.[6–11] Overall, these studies have involved urbanized areas in Europe, North America, and Asia, but there is no information on this association in Latin American countries, where it is recognized that air pollutants concentrations are generally higher than in North America and Europe.[4,22] Uncertainty therefore remains as to whether the same effect is observed in different geographical areas and what its magnitude is. In addition, the effect of air pollution on COPD in Bogotá, a large city located at high altitude (2640 m) in a tropical country, is poorly documented, with only one published retrospective descriptive study.[23]

Bogotá is the most populous city in the world located at high altitude (2640 m) and is situated in a tropical region. The air density is lower, and the ventilation is higher to compensate for the lower oxygen pressure It is recognized as a megacity and has experienced positive population growth because of internal migration and a high birth rate. Bogotá D.C. is home to the country's largest vehicle fleet, with 2,838,874 vehicles registered in 2021.[24] Between 2022 and 2023, the vehicle fleet increased by 4.81% (869,662) and has the highest vehicle density (1000), with a vehicle age of 10 years.[25] Sixty-one percent of $PM_{2.5}$ concentration was generated by mobile sources and 39% by stationary sources.[26]

On the other hand, meteorological conditions resulted in temperature inversions in which a warm atmospheric layer traps other colder ones. This meteorological phenomenon traps and prevents the dispersion of pollutants at ground level, which contributes to the poor air quality in Bogotá.[22]

Bogota has problems with urban mobility, vehicle fleet volume, and population growth that demand more services and energy consumption, factors that contribute to poor air quality and climate change.

Moreover, little is known about the long-term effects of air pollution on COPD, especially $PM_{2.5}$ and NO_2. To date, the published literature reports the short-term[27–35] and long-term[32,36–39] effects of air pollution on hospital admissions caused by COPD-E. Very few studies have evaluated the long-term effects of air pollution on the exacerbation frequency spectrum. Furthermore, addressing the COPD-E related to air pollution exposure is relevant given the increasing stationary and mobile sources of air pollution as well as the sustained use of fossil fuels by anthropogenic activities and other energy consumption. This study aimed to determine the association between long-term exposure to $PM_{2.5}$ and NO_2 and the incidence of COPD-E in patients belonging to AIREPOC, an institutional integrated care program for COPD, in Bogota, Colombia, between 2018 and 2021.

Materials and Methods

Study Design and Population

The AIREPOC Program includes patients with COPD of the Fundación Neumológica Colombiana, a specialized tertiary care facility, in the capital district of Bogota, Colombia. All patients have a clinically and spirometry (forced expiratory volume in one second/forced vital capacity ratio [FEV_1/FVC] below the lower limit of normal) confirmed diagnosis of COPD and receive a personalized integrated and continuous management (AIREPOC cohort). This is a retrospective longitudinal study of adults aged 32 to 97 years at the time of recruitment between 2018 and 2021. A total of 722 participants with a diagnosis of COPD were identified from the clinical records of the AIREPOC program. For each of them, demographic, risk factors, medical history, spirometry, including Global Initiative on Obstructive Lung Disease (GOLD) classification[40] and exacerbation information, were available, and were complemented by information from national health system records, including hospitalizations and COVID-19 infections. COPD exacerbations were verified in patients' clinical records.

This study was approved by the Ethics Committee of the National School of Public Health of the University of Antioquia (CEI- 21030002-00162) and the ethics committee of the Fundación Neumológica Colombiana. Patients at AIREPOC entry gave written informed consent to use their data in research studies. The present study complies with the ethical principles of human subjects research and the Declaration of Helsinki.

Air Pollution Measurements and Exposure Estimation

Environmental air pollution exposure information was provided by the Environment Secretary of Bogotá based on data from the Air Quality Monitoring Network, which consists of 20 air quality monitoring stations. Data obtained for the stations included the daily average of air pollutants and meteorological variables, for the study period. Daily estimations for air pollutants were calculated when the temporal representativeness ≥75% of the hourly record for each pollutant.

The exposure levels of air pollutants were assigned based on the residential addresses and the location of the air quality monitoring stations that were assumed as centroids of circular buffers of 5 km and 10 km. Daily estimations for each residential address were estimated by using the Inverse Distance Weighted Squared (IDWR) method.[40–44] Linkage of environmental data to cohort participants was conducted by using COPD-E dates and locations of participants' home addresses. For the estimation of long-term exposure to air pollutants, annual means for $PM_{2.5}$, NO_2, and meteorological variables were calculated for each patient in the cohort for the four years of follow-up. Air pollutants were recorded on a 24-hour basis for four years of study from air monitoring stations. The air pollutant concentrations were converted to quartiles of exposure for each pollutant.

Outcome Variable

We determined the frequency of COPD-E during the study period as the main outcome variable. Exacerbations requiring additional pharmacological intervention (steroids and/or antibiotics) or emergency visits or hospitalizations were considered. Information about the date of occurrence and length of hospitalization was obtained from the clinical records of the AIREPOC program. The previous history of COPD-E was determined by the registry of daily counts of hospital admissions or outpatient managed exacerbations during 2017 and verified from clinical records. Information was complemented from the COPD-E identified by the National Health System using the International Statistical

Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code ICD-10: J44.1, J440. Patients from AIREPOC gave written informed consent to use their data in research studies during their first clinical visit.

Statistical Analysis

Negative binomial regression truncated at zero was used to estimate the coefficient and the 95% confidence interval (95% CI) associated with categories of exposure with cutoffs at 15 μg/m^3 for $PM_{2.5}$ and 25 μg/m^3 for NO_2, corresponding to intermediate objectives of the WHO 2021 guidelines.[3] Associations were evaluated using the Kruskal–Wallis test. The Akaike's Information Criterion (AIC) was used to select the variables to be included in the models. The goodness-of-fit of the model was assessed by residual analysis. Collinearity was assessed by the Variance Inflation Factor (VIF). All significance tests were conducted with a 95.0% significance. Data were processed using the R statistical package, version 4.3.2 R Core Team, 2023.[45]

Results

Characteristics of the AIREPOC Cohort Participants

The cohort included 722 participants from the AIREPOC program with an age average of 75.1 years old and confirmed COPD diagnosis. During the four years of follow-up, 580 episodes of COPD-E occurred in 382 (52.9%) participants for a ratio of 1.52 COPD-E/person. Among participants, the mean pre-bronchodilator FEV_1 and FVC were 1.37 and 3.14 liters, respectively.

Participants who developed COPD-E were more likely to be married, be classified in groups C and D according to GOLD 2019, with higher depression according to the Brief Patient Health Questionnaire (PHQ-9), more anxiety measured by Beck scale, fewer meters walked according to the 6-minute walk, with lower quality of life according to the Saint George scale, and with higher severity of COPD symptoms by the Assessment Test or CAT scale (Table 1) (Figure S1).

Exposure to Air Pollution

The mean air pollutant levels of $PM_{2.5}$ and NO_2 estimated for the cohort patients were 16.02 ± 4.36 μg/m^3 and 30.34 ± 6.89 μg/m^3, respectively. During the follow-up period, statistically significant decreases in annual $PM_{2.5}$ and NO_2 concentrations were observed. The averages of the meteorological variables were 14.73 ± 0.5 °C for temperature, 161.19 ± 15.78 W/m^2 for solar radiation, and 65.44 ± 2.17% for relative humidity over the period (Table 1). Spearman

Table 1 Characteristics of the Participants of the 2018–2021 AIREPOC Cohort

Characteristics	All N=722 n (%)	n
Exacerbations of COPD (COPD-E)		722
Patients without COPD-E	340 (47)	
Patients with any exacerbation*	382 (53)	
One COPD-E	262 (37)	
Two COPD-E	74 (11)	
Three COPD-E	30 (5)	
More than four COPD-E	16 (3)	
* 382 patients with 580 exacerbations		
Sex		722
Male	434 (60.1)	
Female	288 (39.9)	
Age at baseline ($\bar{x} \pm DE$)	75.1 ± 9.50	
COPD classification (GOLD 2019)		722
Grade A	202 (28.0)	
Grade B	285 (39.5)	
Grade C	79 (10.9)	
Grade D	156 (21.6)	

(*Continued*)

Table 1 (Continued).

Characteristics	All N=722 n (%)	n
Pulmonary function ($\bar{x} \pm DE$)		
FVCpre-BD (L)	2.66 ± 2.72	702
FEV_1pre-BD (L)	1.30 ± 0.54	702
FEV_1/FVC pre-BD	0.49	
FVC pos-BD	3.14 ± 9.56	702
FEV_1 pos-BD	1.81 ± 0.52	693
FEV_1/FVC pos-BD	0.58	699
Saint George Quality of Life Questionnaire ($\bar{x} \pm DE$)		
Symptoms	41.0 ± 23.75	
Activity	60.2 ± 34.2	
Impact	32.9 ± 21.90	
Total	42.4 ± 18.72	
Risk factors: (%)		722
Wood smoke	93 (12.9)	
Tobacco and other smokes	419 (58.0)	
Wood smoke	182 (25.2)	
Passive smoking	20 (2.8)	
No risk factor	8 (1.1)	
Current smoking (%)		709
No	644 (90.8)	
Yes	64 (9.03)	
NA	1 (0.14)	
Index Packages Year (IPA) ($\bar{x} \pm DE$)	35.0 (28.02)	622
Categorized Packages Year Index (PPI) (%)		722
Mild < 5	100 (13.9)	
Moderate 5–15	297 (41.1)	
Severe 16–25	169 (23.4)	
Very Severe >25	156 (21.6)	
COVID-19 (%)		
No		
Yes		
Depression PHQ9 ($\bar{x} \pm DE$)		
COVID-19 (%)		
No		
Yes		
Air pollutants and meteorological variables		722
$PM_{2.5}$ (ug/m^3) ($\bar{x} \pm DE$)	16.0 ± 4.36	722
NO_2 (ug/m^3) ($\bar{x} \pm DE$)	30.3 ± 6.89	722
Temperature (°C) ($\bar{x} \pm DE$)	14.7 ± 0.50	722
Precipitation (mm) ($\bar{x} \pm DE$)	0.11 ± 0.04	722
Solar radiation (Wm^2) ($\bar{x} \pm DE$)	161 ± 15.78	722
Relative humidity ($\bar{x} \pm DE$)	65.4 ± 2.17	722

Abbreviations: (%), Percentage; ($\bar{x} \pm DE$), Mean and standard deviation; FVC pre-BD, Forced Vital Capacity pre-bronchodilator; FEV_1pre-BD, Forced Expiratory Volume in the first-second pre-bronchodilator; FEV_1/FVC pre-BD, FEV_1/FVC pre- bronchodilator ratio; FVC pos-BD, Forced Vital Capacity post-bronchodilator; FEV_1 pos-BD, Forced Expiratory Volume in the first second post-bronchodilator; FEV_1/FVC pre-BD, Ratio FEV_1/FVC pre-bronchodilator; FEV_1/FVC pos-BD, Ratio FEV_1/FVC post bronchodilator; Saint George Quality of Life, Questionnaire that rates the impact of airway diseases on health status and well-being; PHQ-9, Patient Health Questionnaire (Screening of patients with depressive disorder); $PM_{2.5}$, Particulate Matter smaller than 2.5 μm in μg/m^3; NO_2, Nitrogen dioxide in μg/m^3.

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correlation coefficients were strongest between the two study pollutants (r_s = 0.62), followed by $PM_{2.5}$ and temperature (r_s = 0.49) and $PM_{2.5}$ and solar radiation (r_s = 0.38). The correlation of $PM_{2.5}$ and NO_2 with the number of COPD-E events was 0.06 and −0.02, respectively. The spatial distribution of exposure to $PM_{2.5}$ μg/m^3 and NO_2 μg/m^3 for each patient in the AIREPOC program from 2018 to 2021 can be seen in Figure S2.

In the single pollutant models (Table 2), long-term exposure to NO_2 was associated with increased COPD-E frequency, adjusted for COPD severity, relative humidity, and solar radiation. In both models, adjusting for the forced expiratory volume in the first-second (FEV_1) was not significant. Those patients exposed to concentrations ≥25 μg/m^3 compared to those exposed to levels <25 μg/m^3 of NO_2 increased the frequency of COPD-E by 29% (95% CI 2%–67%). In contrast, there was no statistically significant association between COPD-E and $PM_{2.5}$ concentrations equal or higher than 15 μg/m^3.

The goodness-of-fit test shows that the predicted values are similar to those observed for all regressions (Table 3). Both models, for $PM_{2.5}$ and NO_2, show that the values of the Variance Inflation Factor (VIF) did not exceed the magnitude of 10; consequently, there was no collinearity (Table 3).

No significant interaction was found for temperature, $PM_{2.5}$, and NO_2. In the stratified analysis by sex, similar associations were found with statistically significant associations between COPD-E and NO_2 exposure for males (RDI:1.57, 95% CI:1.05–2.35) and absence of association for women. For $PM_{2.5}$ neither sex, males and females, showed association with the frequency of COPD-E Tables S1 and S2.

Table 2 Variables Associated With Frequency of COPD Exacerbations; Negative Binomial Model Truncated at Zero

	$PM_{2.5} \geq 15$ μg/m^3				$NO_2 \geq 25$ μg/m^3			
Variables	**IDR**	**95CI%lower limit**	**95CI% upper limit**	**Value of P**	**IDR**	**95CI% lower limit**	**95CI% upper limit**	**Value of P**
Contaminant	0.99	0.97	1.01	0.000	1.29	1.02	1.67	0.005
Grade B	0.83	0.62	1.06	0.895	0.79	0.60	1.04	0.071
Grade C	1.64	1.21	2.24	0.004	1.62	1.19	2.20	0.001
Grade D	1.83	1.41	2.40	0.000	1.76	1.34	2.30	0.000
Depression	1.01	0.98	1.02	0.652	1.01	0.98	1.02	0.415
FEV1 pre bronchodilator	1.01	0.84	1.19	0.447	1.04	0.84	1.19	0.493
Relative humidity	0.87	0.83	0.91	0.000	0.88	0.84	0.92	0.000
Solar radiation	1.01	1.01	1.02	0.000	1.01	1.01	1.16	0.001

Notes: Comparison group: patients exposed to levels <25 μg/m^3 of NO_2 patients exposed to levels <15 μg/m^3 of $PM_{2.5}$.
Abbreviations: IDR, Incidence density rate; CI, Confidence intervals.

Table 3 Goodness-of-Fit Comparison of Zero-Truncated Negative Binomial Models

Indexes	**$PM_{2.5}$**	**$PM_{2.5} \geq 15$ μg/m^3**	**NO_2**	**$NO_2 \geq 25$ μg/m^3**
Log-Likelihood	−645.69	−657.11	−653.28	−655.13
AIC	1315.41	1334.22	1330.58	1330.26
Collinearity	No hay	No hay	No hay	No hay
RMSE	96.78	27.56	24.41	26.91

Abbreviations: AIC, Akaike information criterion; RMSE, Root mean square Error.

Discussion

An association was observed between long-term air pollution exposure and COPD-E frequency. Individuals with chronic exposure to concentrations of $NO_2 \geq 25$ μg/m^3 had 29% (95% CI: 2%-67%) increase in the incidence rate of COPD-E frequency. However, no such association was observed for concentrations of $PM_{2.5} \geq 15$ μg/m^3.

In addition, NO_2 exposure was found to be more strongly associated with the frequency of COPD-E in patients classified as GOLD C/D (exacerbator patients), with lower ambient relative humidity, and in people with exposure to higher levels of solar radiation. There was no association with pre-bronchodilator FEV_1 value or depression status. This may be partly due to the limited sample size of people with depression.

It was also found that, in the sex-stratified analysis, we found a stronger association for NO_2 concentrations among males, with an increased risk in the frequency of COPD-E of 57% (95% CI 5–135%), while no association was evident for NO_2 concentrations in females. Absence of associations among females might be partly explained by the limited sample size of COPD-E frequency cases in this group.

In the context of our current knowledge of the known adverse respiratory effects of prolonged exposure to NO_2 air pollution,[46] our findings are consistent with some studies[9,37,47–51] reporting that COPD patients are more likely to suffer COPD-E related to increased levels of $PM_{2.5}$ and NO_2 air pollution. However, no studies were found in the current literature that demonstrated an association between the frequency of COPD-E and chronic exposure to $PM_{2.5}$ and NO_2. Given the scarcity of literature on this topic, these findings may serve as knowledge for future research.

At the time of the study, only the study by Morantes and Fajardo, in 2019 in Bogotá D. C, reported that high concentrations of $PM_{2.5}$ and PM_{10} with 48-hour lag (lag 2) were associated with increased sputum volume (OR: 4.74; 95% CI:1.02–21.90), purulence (OR: 6.58;95% CI:2.51–17.20), pleuritic pain (OR:3.62;95% CI:1.27–10.37), antibiotic use (OR:2.87;95% CI:1.17–7.07) and corticosteroids (OR:2.62;95% CI:1.07–6.44).[23]

A new finding identified the association between the frequency of COPD-E and prolonged exposure to $PM_{2.5}$ and NO_2 in patients with higher solar radiation exposure, worse COPD severity according to GOLD C/D, and lower relative humidity. These variables have not been investigated in previous epidemiological studies of short- and long-term effects. Only two studies from Ferrari et al[52] and Huh et al,[53] documented the negative effect of solar radiation, temperature, and relative humidity on COPD-E.

Our findings are consistent with current knowledge about biological plausibility connecting air pollutants exposure and COPD. It is known that biological mechanisms may differ between short-term and long-term exposure to air pollution in COPD patients. Short-term exposure increases Th1 and Th17 cytokines while decreasing Th2 cytokines,[54] which may trigger acute airway inflammation and exacerbation,[55] leading to death,[55,56] whereas long-term exposure leads to airway remodeling, fibrosis, and smooth muscle hyperplasia[55] resulting in COPD progression[57] and disease exacerbation.[54] Particulate matter may exacerbate inflammation by inducing epithelial remodeling and dendritic cell dysfunction in COPD patients.[54,58]

The high solar intensity has been associated with melatonin depletion, which may be responsible for adverse health effects in COPD patients by increasing inflammation and oxidative stress activity in the lung.[59] The melatonin in the lung modulates proinflammatory cytokines such as interleukin 1β and 6, and tumor necrosis factor-alpha (TNF-α).[59] The intensity of solar radiation can also affect by disrupting the 24-hour circadian rhythm and the physicochemical properties and toxicity of gaseous pollutants.[59]

In addition, a significant relationship between inflammatory markers and $PM_{2.5}$ and NO_2 has been observed, as evidenced by Squillacioti et al.[60] Both in vitro and in vivo animal studies have shown the systemic inflammatory effect mediated by oxidative stress and lung inflammation from both short- and long-term exposure to NO_2 and $PM_{2.5}$.[60–63] The main source that generates NO_2 is fuel burning by vehicles, in addition to other sources such as power plants and agriculture, its concentration is higher in urban areas and is considered a marker of traffic-related air pollution mixing.[64] In Bogota, 69% of $PM_{2.5}$ emissions were due to resuspension; emissions from on-road mobile sources contribute 89% by NO_x and 22% by $PM_{2.5}$.[65] In addition, NO_X contributes to the formation of other pollutants such as ozone and other secondary particulate matter. Consequently, an increase in NO_2 reacts with other pollutants and dissipates faster than $PM_{2.5,}$ NO_2 levels can vary depending on traffic patterns[64] and meteorological variables. Evidence suggests that NO_2 and

PM_{10}, $PM_{2,5}$ exposure increases acute systemic inflammation in patients with COPD,[3,60,66,67] which could lead to the accumulation of disease exacerbations resulting in a long-term increase in the frequency of COPD-E.

NO_2 could be pathophysiologically related with COPD exacerbations because it promotes the production of free radicals such as reactive oxygen species (ROS), the which could add to the fact that in people with respiratory diseases the antioxidant function is compromised, making it ineffective against ROS aggressions.[60]

This study had several limitations. First, the effect of other pollutants was not assessed, because the data did not meet the criterion of temporal representativeness. Second, a measurement bias is possible in the estimation of individual exposure because air pollution data and urban meteorological factors may differ from individual mobility exposure levels and may not represent the total exposure of the cohort; however, participants were older than 75 years, which implies they probably spent most of the time at home. In addition, the potential information bias of exposure misclassification was controlled by geolocating the participants' addresses more than eight times.

If coding errors occurred, they would be random and should not be a valid argument for non-differential misclassification, which would bias the study results toward the null. Third, records in the AIREPOC program included incomplete data; however, missing values were less than 15% for spirometry parameters (2.77%), dyspnea (1.24%); arterial gases (9.4%), COPD severity classification by GOLD (11.77%); and IPA (13.05%). We used real-world data that allow for external validity and generalizability due to their volume and long follow-up, thus reducing clinical uncertainty.[68] However, by selecting a subset of people with COPD participating in a specialized institutional program, it could lead to selection bias. We believe that patients with COPD who are not participants in specialized programs such as AIREPOC are probably in poorer clinical conditions and living in more polluted areas of the city and therefore might be more susceptible to the effects of air pollutants. Thus, the potential selection bias in our cohort is probably underestimating the effect measure of association between air pollutants and frequency of COPD-E in the general population of COPD patients in Bogotá.

The main strengths of our study are related to the following aspects: the use of real-life data that fully capture care throughout the follow-up period and include information for important covariates such as smoking, occupational exposure, validated scales measuring the quality of life, depression, anxiety, history of exacerbation, and occupational exposure. The use of the long-term estimates of air pollutant's concentration reduces the potential exposure measurement bias compared to short-term studies as the temporal variations in the monthly and annual exposure averages are smaller. Another important strength was the use of a standardized definition of COPD-E validated by GOLD.[69]

Our results provide evidence that improving air quality in Bogota could reduce the burden of COPD-E frequency, the prognosis of the disease, and improve the COPD control related to air pollution etiotype. For achieving this goal, it is necessary to involve patients and local stakeholders in the management of health risks in the COPD population, provide training for health professionals on the effects and health risks of exposure to air pollution and use different media to communicate the risks to the general population and COPD patients.[70]

The results of this research highlight the importance of continuing with regulatory efforts to reduce air pollution emissions and environmental education for the susceptible population, as well as for health personnel to learn about evidence-based recommendations on air pollution; the inclusion of a real-time health and environmental epidemiological surveillance system to identify air pollution episodes in a timely and effective manner, promote citizen oversight, and the community should acquire environmental habits such as using public transportation, carpooling, walking or using electric vehicles, performing preventive maintenance on vehicles, using clean energy for cooking and avoiding open burning.[71]

Conclusion

This cohort study shows evidence of significant associations between air pollution and increased risks of COPD-E frequency among patients participating in a specialized rehabilitation program in Bogotá. Long-term NO_2 exposures were associated with higher exacerbation frequency. In addition, this work provides novel findings that prolonged exposure to NO_2, together with the effect of high solar intensity, higher severity of COPD, and lower relative humidity, increase the risk of COPD frequency.

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Disclosure

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