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COVID-19 Lockdown Air Pollution Reduction: Did It Impact the Number of COPD Hospitalizations?

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Abstract: In addition to the detrimental health consequences, the early stages of the COVID-19 pandemic have yielded unforeseen benefits in terms of reducing air pollution emissions. This study investigated air pollution changes in Novi Sad, Serbia, during the COVID-19 lockdown (March–June 2020) and their correlation with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) hospitalizations. Using quasi-Poisson generalized linear models (GLM) and distributed lag non-linear models (DLNM), we examined the relationship between the number of AECOPD hospitalizations and the concentrations of selected air pollutants (PM_{10}, $PM_{2.5}$, SO_2, and NO_2) from March to June of 2019, 2020, and 2021. During the COVID-19 lockdown, significant reductions in most air pollutant concentrations and the number of AECOPD hospitalizations were observed. However, neither the study year nor its interaction with air pollutant concentration significantly predicted AECOPD hospitalizations ($p > 0.05$). The 95% confidence intervals of the relative risks for the occurrence of AECOPD hospitalizations at each increase in the examined air pollutant by 10 $\mu g/m^3$ overlapped across years, suggesting consistent effects of air pollution on the risk of AECOPD hospitalizations pre-pandemic and during lockdown. In conclusion, reduced air pollution emissions during the COVID-19 lockdown did not lead to a statistically significant change in the number of AECOPD hospitalizations.

Keywords: COVID-19 lockdown; acute exacerbations of chronic obstructive pulmonary disease; air pollution

1. Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has emerged as the most significant global concern for humanity in recent decades. In spite of the severe health implications, the early stages of the COVID-19 pandemic yielded unforeseen benefits in terms of mitigating air pollution emissions and curbing energy usage [1,2]. This was due to the implementation of self-isolation and social distancing measures, movement restrictions, and a reduction in traffic and industrial activity, all in order to prevent the transmission of the infection [3]. Hence, one study determined that during the COVID-19 lockdown in India, PM_{10} (particulate matter $\leq$10 μm in diameter) concentrations decreased by 55%, $PM_{2.5}$ (particulate matter $\leq$2.5 μm in diameter) concentrations decreased by 49%, NO_2 (nitrogen dioxide) concentrations decreased by 60%, and SO_2 (sulfur dioxide) concentrations decreased by 19% [4]. Similar findings regarding the decline in particulate and gaseous air pollutant concentrations were observed in studies conducted in Thailand [5], Egypt [6], China [7], and Serbia [8]. The health benefits of such reduced air pollution emissions on the decrease in overall morbidity and mortality were promptly demonstrated by several studies [8–10].

Air pollution is currently the most significant external risk factor for human health globally, contributing to the onset of numerous chronic diseases in adults and children (mainly respiratory, cardiovascular, neuro-degenerative and malignant diseases) [11]. Additionally, it can exacerbate existing chronic conditions and lead to acute episodes, ultimately resulting in adverse health outcomes. Exposure to air pollution can affect the onset and progression of chronic obstructive pulmonary disease (COPD) [12]. While various toxic substances contribute to air pollution, studies have identified particulate matter (PM) and gaseous pollutants (such as SO_2, ozone (O_3), and NO_2) as primary contributors to the development of acute exacerbations of chronic obstructive pulmonary disease (AECOPD). The short-term exposure to these pollutants leads to increased emergency medical service interventions, outpatient visits, hospitalizations, and ultimately, a rise in COPD-related mortality [12–16]. COPD ranks third among all causes of death attributable to air pollution [17]. The mechanisms through which air pollutants contribute to AECOPD development involve inducing oxidative stress and inflammation in the airways, airway hyperreactivity, and a reduction in the effectiveness of local protective mechanisms [18]. Therefore, any intervention aimed at reducing air pollution concentrations could potentially have a beneficial impact on the morbidity and mortality associated with AECOPD.

Considering this, the primary objective of our study was to determine whether there was a reduction in air pollution emissions on the territory of the City of Novi Sad, Serbia, during the initial months of the COVID-19 pandemic (lockdown period), as well as whether exposure to air pollution in that period affected the risk for the development of AECOPD hospitalizations of non-infectious etiology.

2. Materials and Methods

This time-series is part of a larger research project examining the impact of air pollution and meteorological factors on the frequency, mortality, and clinical course of non-infectious AECOPD hospitalizations of patients from the City of Novi Sad, Serbia, who were treated at the Institute for Pulmonary Diseases of Vojvodina (IPDV).

2.1. Study Time Frame

The first case of COVID-19 infection in the Republic of Serbia was recorded on 6 March 2020, followed shortly thereafter by the implementation of a lockdown period aimed at preventing the spread of the COVID-19 infection. The lockdown period lasted until June 2020. Considering the objectives of this study, we collected average daily concentrations of selected air pollutants and the number of AECOPD hospitalizations of non-infectious etiology that were realized at the IPDV during the period from March to June 2020 (during the COVID-19 lockdown), as well as during the same period in 2019 (the pre-pandemic year) and 2021 (the second pandemic year without a lockdown).

2.2. Study Population

The study sample consisted of hospitalizations of patients with non-infective AECOPD that occurred during the aforementioned time period at IPDV. IPDV is a reference healthcare, educational, and research institution serving all patients residing in the territory of the City of Novi Sad. Inclusion study criteria were: residency of hospitalized patients within the territory of the City of Novi Sad, previous diagnosis of COPD, hospitalization due to AECOPD, and based on laboratory and bacteriological analyses upon admission, it was assessed that AECOPD was caused by a non-infective agent.

2.3. Study Location and Air Pollution Data

This study analyzed the AECOPD hospitalizations of patients residing in the territory of the City of Novi Sad. Novi Sad is the capital and the main economic, cultural, tourist, sports, scientific, and industrial center of the Serbian autonomous province of Vojvodina. It is situated on the Danube River's course through Serbia. A part of the city on the left bank of the Danube lies in the Pannonian Plain, while on the right bank stretches the mountain massif of Fruška Gora (up to 250 m above sea level). Novi Sad belongs to the urban-industrial type of agglomeration, with administrative and business facilities, as well as residential buildings, concentrated in the city's central area. In the peripheral parts of the agglomeration, there are individual residential buildings as well as facilities intended for commercial and industrial activities (especially on the northern side of the city). Green areas are distributed along the banks of the Danube River, as well as in parks and suburbs within the city. The city has a dense traffic network of main and secondary roads, with incompletely developed transportation infrastructure on the outskirts, along with numerous agricultural and forested areas [19].

During the selected temporal interval, mean 24-h concentrations (expressed in $\mu g/m^3$) of the air pollutants selected for this investigation (PM_{10}, $PM_{2.5}$, SO_2, and NO_2) were systematically gathered from monitoring stations strategically positioned throughout the urban landscape of the City of Novi Sad. These stations are strategically located to discern air pollution primarily attributed to proximal emission sources, notably vehicular traffic (urban traffic, UT), and ambient air pollution typical of residential urban locales, stemming from diverse pollution sources (urban background, UB). Figure 1 depicts the spatial configuration of monitoring stations utilized for sampling air pollutant concentrations within the Novi Sad metropolitan region.

The standard gravimetric measurement method was used to determine the average daily concentration of PM_{10} or $PM_{2.5}$ in the ambient air, in accordance with the standardized method SRPS EN 12341:2015. Measurements were performed using the Sven Leckel LVS3 air sampling device, with a specially designed inlet operating at a nominal flow rate of 2.3 m^3/h, during a nominal sampling period of 24 h [19]. The determination of SO_2 concentration in 24-h air samples was conducted in accordance with SRPS ISO 4219:1997 and points 1, 2, 3, and 7 of standard SRPS ISO 4221:1997 using the air sampling devices AT-801 and AT-801x2. Additionally, continuous, automatic measurement was carried out in accordance with standard SRPS ISO 14212:2013/AC:2015 using the measurement instrument API Teledyne T100 snl 621 [20]. The determination of NO_2 concentration in 24-h air sampling was conducted in accordance with the Sampling and Determination Instructions for Nitrogen Dioxide Q3.XИ.341 (spectrophotometric method) using the air sampling device AT 801x2. Furthermore, automatic 24-h continuous measurement of NO_2, nitrogen monoxide, and nitrogen oxide (NOx) concentrations was conducted in accordance with standard SRPS EN 14211:2013 using the measurement instrument API Teledyne T200 sn 2045 [20].

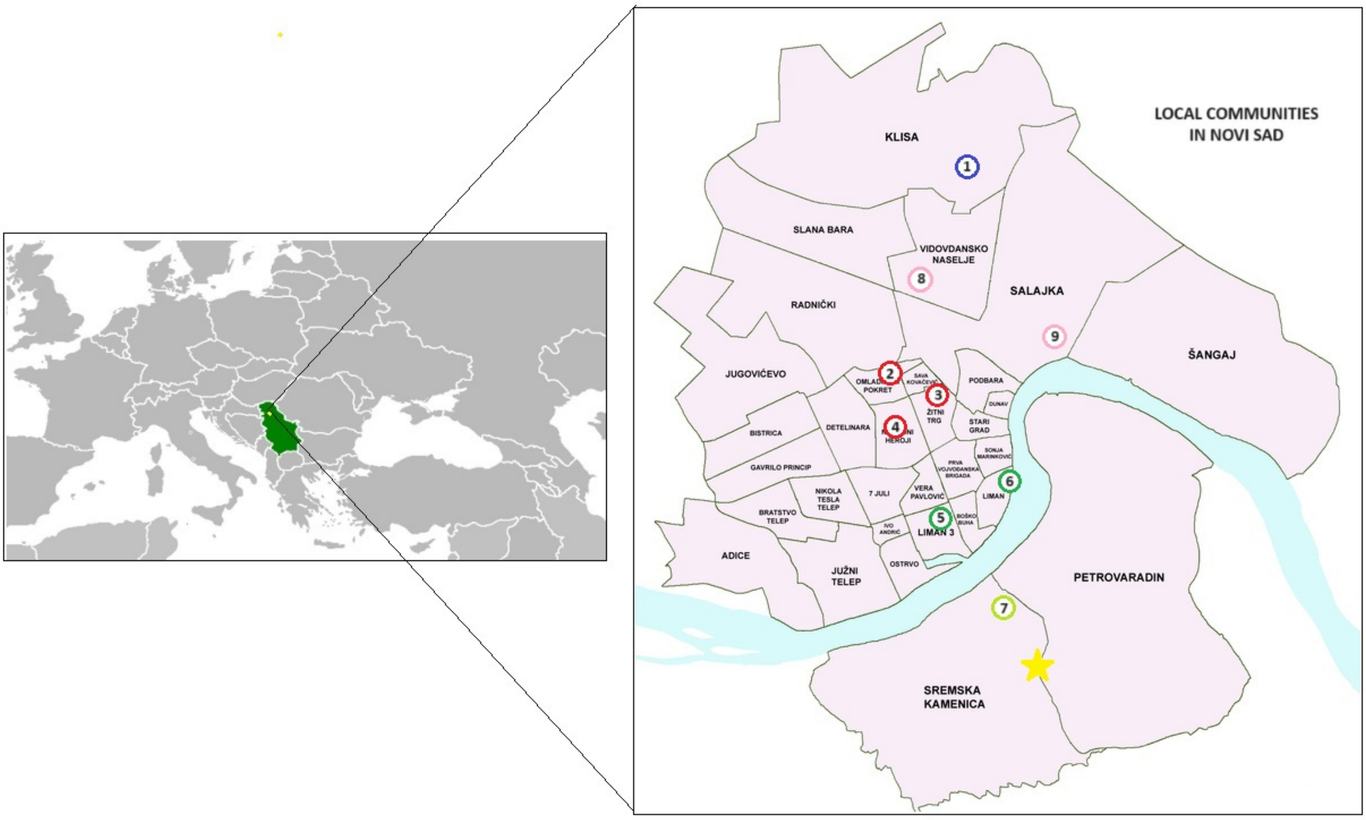

Figure 1. The network of stations for collecting data on meteorological factors and air pollution inside the local communities of the City of Novi Sad. Legend: meteorological station (marked in blue circle): 1 (45°20′ N, 19°51′ E); air pollution stations: detecting urban traffic air pollution (marked in red circles)—2 (45°15′ N, 19°49′ E), 3 (45°25′ N, 19°83′ E), and 4 (45°24′ N, 19°81′ E); detecting urban background air pollution (marked in green circles)—5 (45°14′ N, 19°50′ E) and 6 (45°25′ N, 19°85′ E); detecting suburban background air pollution (marked in light-green circle)—7 (45°13′ N, 19°50′ E); detecting suburban industrial air pollution (marked in pink circle)—8 (45°16′ N, 19°52′ E) and 9 (45°29′ N, 19°78′ E); yellow star—localization of the Institute for the Pulmonary Diseases of Vojvodina (45°21′ N, 19°85′ E).

2.4. Statistical Analysis

In order to achieve the goals of our study (effects of exposure to air pollution on the risk of AECOPD hospitalizations during the COVID-19 lockdown), a quasi-Poisson generalized linear model (GLM) and a distributed lag nonlinear model (DLNM) were implemented. GLMs were first constructed for each of the observed predictors, where the concentrations of air pollutants (PM_{10}(UB), PM_{10}(UT), $PM_{2.5}$(UB), $PM_{2.5}$(UT), SO_2(UB), SO_2(UT), NO_2(UB), and NO_2(UT)) and the number of AECOPD admissions during 2019, 2020, and 2021 were analyzed. The year of study was included as a confounding variable in the used formulas (if this factor was statistically significant, it indicated that the number of AECOPD admissions significantly differed across the three observed years), along with the interaction between predictors and year (the statistically significant effect of this interaction would suggest that the effect of predictors significantly varied depending on the year), whether admission occurred on weekdays or weekends, and the natural spline of dates for controlling seasonal factors. Lag effects were not considered in these analyses, and the relationship between predictors and criteria was treated as linear, as such a relationship was determined to be optimal. Quasi-Poisson regression was used, and the formulas of the models used are as follows:

$$log(g[E(y_t)]) = \alpha + \beta \times PM_{10}(UB)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (1)$$

$$log(g[E(y_t)]) = \alpha + \beta \times PM_{10}(UT)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (2)$$

$$log(g[E(y_t)]) = \alpha + \beta \times PM_{2.5}(UB)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (3)$$

$$log(g[E(y_t)]) = \alpha + \beta \times PM_{2.5}(UT)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (4)$$

$$log(g[E(y_t)]) = \alpha + \beta \times SO_2(UB)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (5)$$

$$log(g[E(y_t)]) = \alpha + \beta \times SO_2(UT)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (6)$$

$$log(g[E(y_t)]) = \alpha + \beta \times NO_2(UB)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (7)$$

$$log(g[E(y_t)]) = \alpha + \beta \times NO_2(UT)_{t,l} + Day + Year + Predictor{:}Year + ns(Date, df = 3), \quad (8)$$

where *yt*—criteria (the dependent variable); *[E(yt)]*—expected number of AECOPD hospitalizations on a certain day *t* during 2019, 2020, and 2021; *log*—link function; α—intercept; β—regression coefficient of the predictor; PM_{10}—average concentration of particulate matter with a size less than or equal to 10 μm in the urban background (UB) or urban traffic (UT) surrounding on day *t*; $PM_{2.5}$—average concentration of particulate matter with a size less than or equal to 2.5 μm in the urban background (UB) or urban traffic (UT) surrounding on day *t*; SO_2—average concentration of sulfur dioxide in the urban background (UB) surrounding on day *t*; NO_2—average concentration of nitrogen dioxide in the urban background (UB) or urban traffic (UT) surrounding on day *t*; Day—predictor (workday or weekend on day *t*); Year—the year of day *t* (2019, 2020 or 2021); Predictor:Year—interaction of the air pollutant and year; ns(Date)—natural spline of dates to control seasonal factors; and df—degree of freedom.

To determine the impact of exposure to air pollution during the COVID-19 lockdown in Serbia (March–June 2020) on the number of AECOPD hospitalizations, we employed DLNM, taking into account the number of AECOPD admissions realized only in the periods equivalent to the 2020 lockdown (periods from March to June of 2019 and 2021). The formulas of the utilized models were identical to those previously mentioned (1–8), excluding the year and the predictor/year interaction as predictors. The relative risk (RR) for AECOPD hospitalization was calculated for each 10 $\mu g/m^3$ increase in the air pollutant concentration. If the 95% confidence intervals (CI) of RR did not overlap, the result could be considered statistically significant. This would indicate that the lower limit of one year's CI is greater than the upper limit of the other year's CI. Before concluding that there was a statistically important difference in the number of AECOPD admissions that could be attributable to air pollution exposure, this would have to be the case for at least one pair of years (2019 and 2020 or 2020 and 2021).

All analyses were performed within R: A language and environment for statistical computing, version 3.0.2 (RC Team, Vienna, Austria, R foundation for Statistical Computing, 2019) utilizing the "dlnm" package [21].

3. Results

Descriptive Statistics

The analysis of medical records revealed 252 AECOPD admissions to IPDV during the examined time frame (period March–June of 2019, 2020, and 2021). After excluding those hospitalizations for which it was determined that the reason for admission was AECOPD caused by an infectious etiology, a total of 112 AECOPD hospitalizations of non-infectious etiology were available for final analysis.

Considering that the COVID-19 lockdown period lasted in Serbia from March to June 2020, Table 1 displays the total number of AECOPD hospitalizations during the March–June period of 2019, 2020, and 2021, which were the years of interest for this specific research. A pairwise comparison revealed a statistically significant difference in the average number of daily AECOPD admissions in the period of March–June between 2019 and 2020 (2020 had significantly fewer admissions, $p = 0.041$), while such a difference was not observed between 2020 and 2021 ($p = 0.715$), although there was a difference in the absolute number of AECOPD hospitalizations (22 hospitalizations in 2020 compared to 41 hospitalizations in 2021).

Table 1. The number of AECOPD hospitalizations during the period of March–June.

Year	AECOPD Hospitalizations		
	Non-Infectious	**Infectious**	**Total**
2019	49	72	121
2020 (lockdown)	22	23	45
2021	41	45	86

Legend: AECOPD—acute exacerbation of chronic obstructive pulmonary disease.

During the observed time periods, the average daily concentrations of air pollutants in the UB environment were: 21.91 μg/m^3 for PM_{10}, 14.90 μg/m^3 for $PM_{2.5}$, 13.99 μg/m^3 for SO_2, and 10.38 μg/m^3 for NO_2 (Figure 2). The average daily concentrations of air pollutants in the UT environment were: 32.01 μg/m^3 for PM_{10}, 18.72 μg/m^3 for $PM_{2.5}$, 14.33 μg/m^3 for SO_2, and 28.01 μg/m^3 for NO_2 (Figure 3). As shown in Table 2, the majority of the examined air pollutants had statistically significant lower concentrations during the lockdown period in Serbia (from March to June 2020) compared to the same period in 2019, while for certain air pollutants, this trend continued into the year 2021.

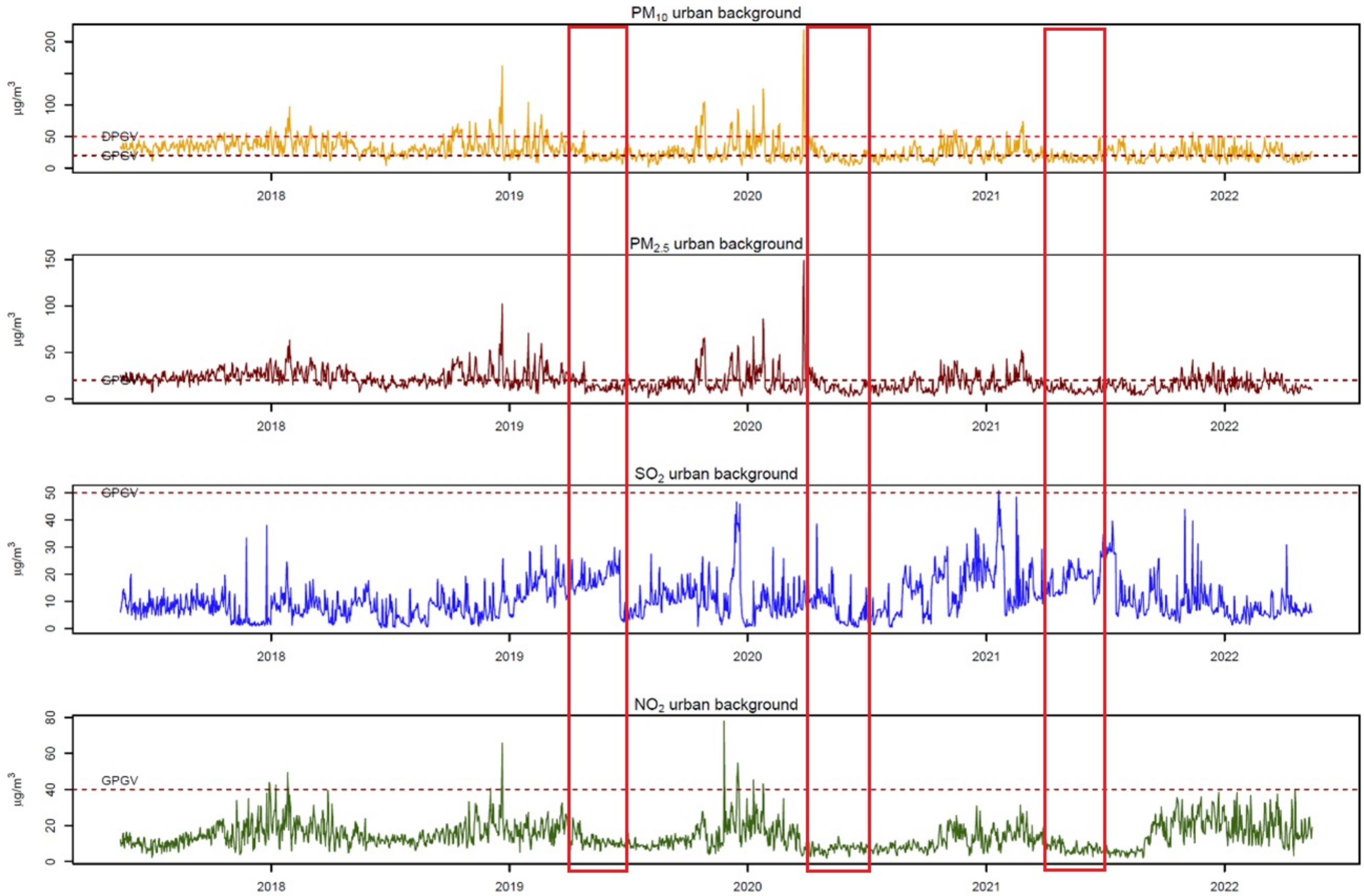

Figure 2. Time series of average daily concentrations of the examined air pollutants in the urban background environment. Legend: red frame—refers to time period of March–June of appropriate year; DPGV—red dashed line indicates the recommended daily concentrations of air pollutants according to Directive 2008/50/EC and the legal acts of the Republic of Serbia; GPGV—dark red dashed line indicates the recommended annual concentrations of air pollutants according to Directive 2008/50/EC and the legal acts of the Republic of Serbia.

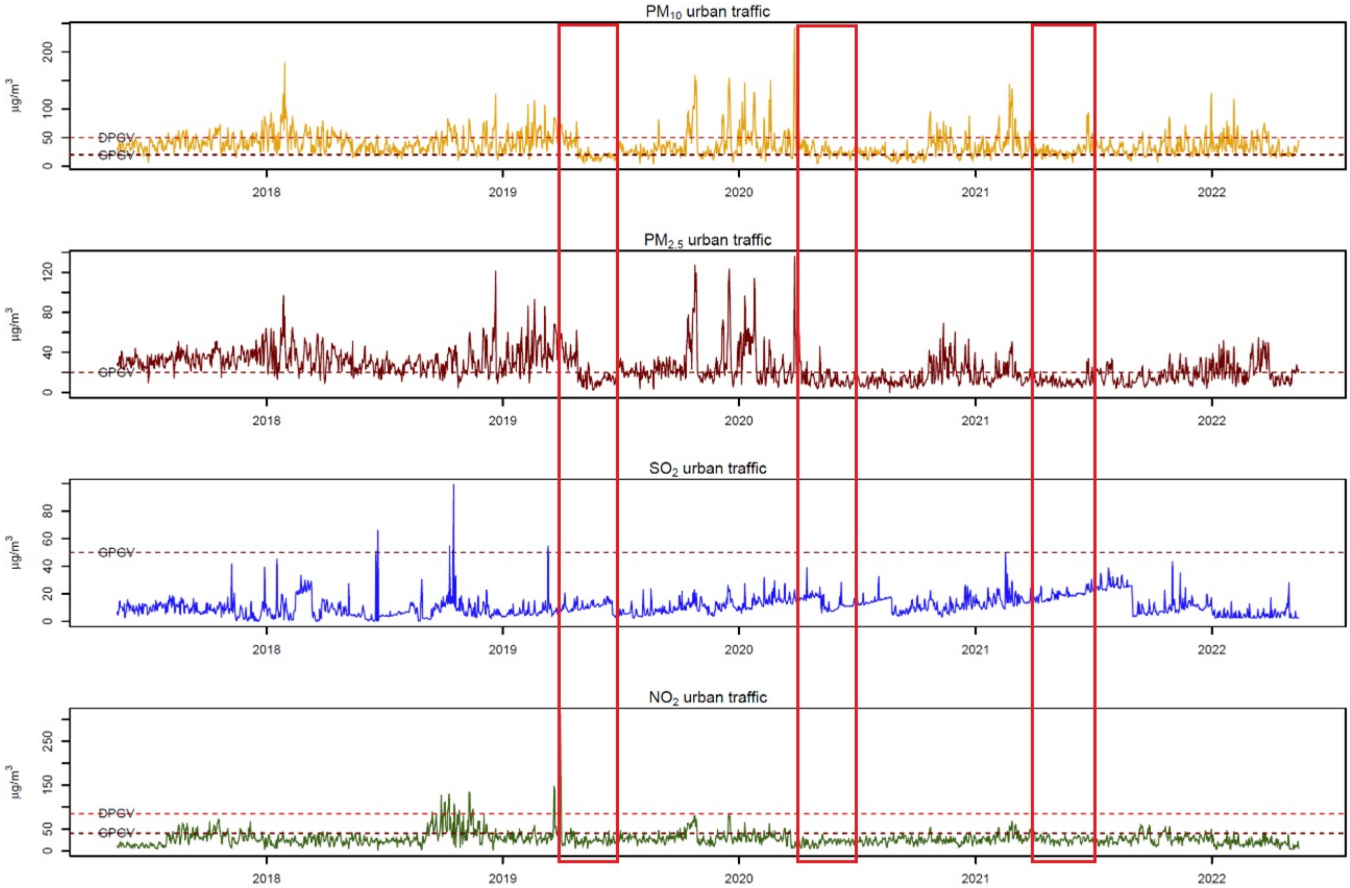

Figure 3. Time series of average daily concentrations of the examined air pollutants in the urban traffic environment. Legend: red frame—refers to time period of March–June of appropriate year; DPGV—red dashed line indicates the recommended daily concentrations of air pollutants according to Directive 2008/50/EC and the legal acts of the Republic of Serbia; GPGV—dark red dashed line indicates the recommended annual concentrations of air pollutants according to Directive 2008/50/EC and the legal acts of the Republic of Serbia.

In the GLM used, the year of admission (2019, 2020, or 2021) and the interaction between the pollutant concentration and year were included as the confounding variables. If these factors were found to be statistically significant, it would imply that the number of AECOPD admissions significantly varied statistically across the observed years or that the effect of the predictor varied statistically significantly by year. In all GLMs, we implemented these; however, these factors lacked statistical significance ($p > 0.05$).

Using DLNM, the RR for AECOPD hospitalization of non-infectious etiology was then calculated for each 10 $\mu g/m^3$ increase in the air pollutant concentration between March and June of 2019, 2020, and 2021. The results are displayed in Figure 4. For two RRs to be statistically significantly different, their 95% CI must not intersect. As shown in Figure 4, all 95% CIs overlap, which indicates that RRs during the three observed periods did not differ statistically significantly, meaning that exposure to air pollution during the lockdown period did not have a statistically significant effect on the change in the number of AECOPD hospitalizations compared to the same period in 2019 and 2021. The illustration pertaining to SO_2(UT) demonstrates that for each 10 $\mu g/m^3$ increase during March–June 2019, the RR for AECOPD hospitalization of non-infectious etiology was 0.05 (95% CI 0.00–7.03), whereas for the same period in 2020, the RR was 1.41 (95% CI 0.03–72.12). Although the calculated RR values are different, the 95% CIs overlap, indicating that there were no statistically significant differences between the effects of SO_2(UT) during these two time periods on the incidence of AECOPD hospitalizations.

Table 2. The average daily concentrations of air pollutants during the period March–June of 2019–2021.

Air Pollutant	March–June			p [a] 2019 vs. 2020	p [a] 2020 vs. 2021
	2019	2020	2021		
PM_{10}(UB) (μm/m^3)	24.64	22.86	18.25	0.08540	0.02672 *
PM_{10}(UT) (μm/m^3)	34.03	31.71	30.30	0.17960	0.30698
$PM_{2.5}$(UB) (μm/m^3)	17.00	15.58	12.12	0.08967	0.01672 *
$PM_{2.5}$(UT) (μm/m^3)	26.86	16.85	12.46	<0.00001 *	0.00162 *
SO_2(UB) (μm/m^3)	16.58	8.14	17.25	<0.00001 *	<0.00001 *
SO_2(UT) (μm/m^3)	10.31	14.58	18.12	<0.00001 *	<0.00001 *
NO_2(UB) (μm/m^3)	13.71	8.20	9.23	<0.00001 *	0.02942 *
NO_2(UT) (μm/m^3)	35.32	20.68	28.04	0.00019 *	<0.00001 *

Legend: PM_{10}—average concentration of particulate matter with a size less than or equal to 10 μm in the urban background (UB) or urban traffic (UT) surrounding; $PM_{2.5}$—average concentration of particulate matter with a size less than or equal to 2.5 μm in the urban background (UB) or urban traffic (UT) surrounding; SO_2—average concentration of sulfur dioxide in the urban background (UB) or urban traffic (UT) surrounding; NO_2—average concentration of nitrogen dioxide in the urban background (UB) or urban traffic (UT) surrounding; [a]—calculated using Student's *t* test; * statistically significant at the level of $p < 0.05$.

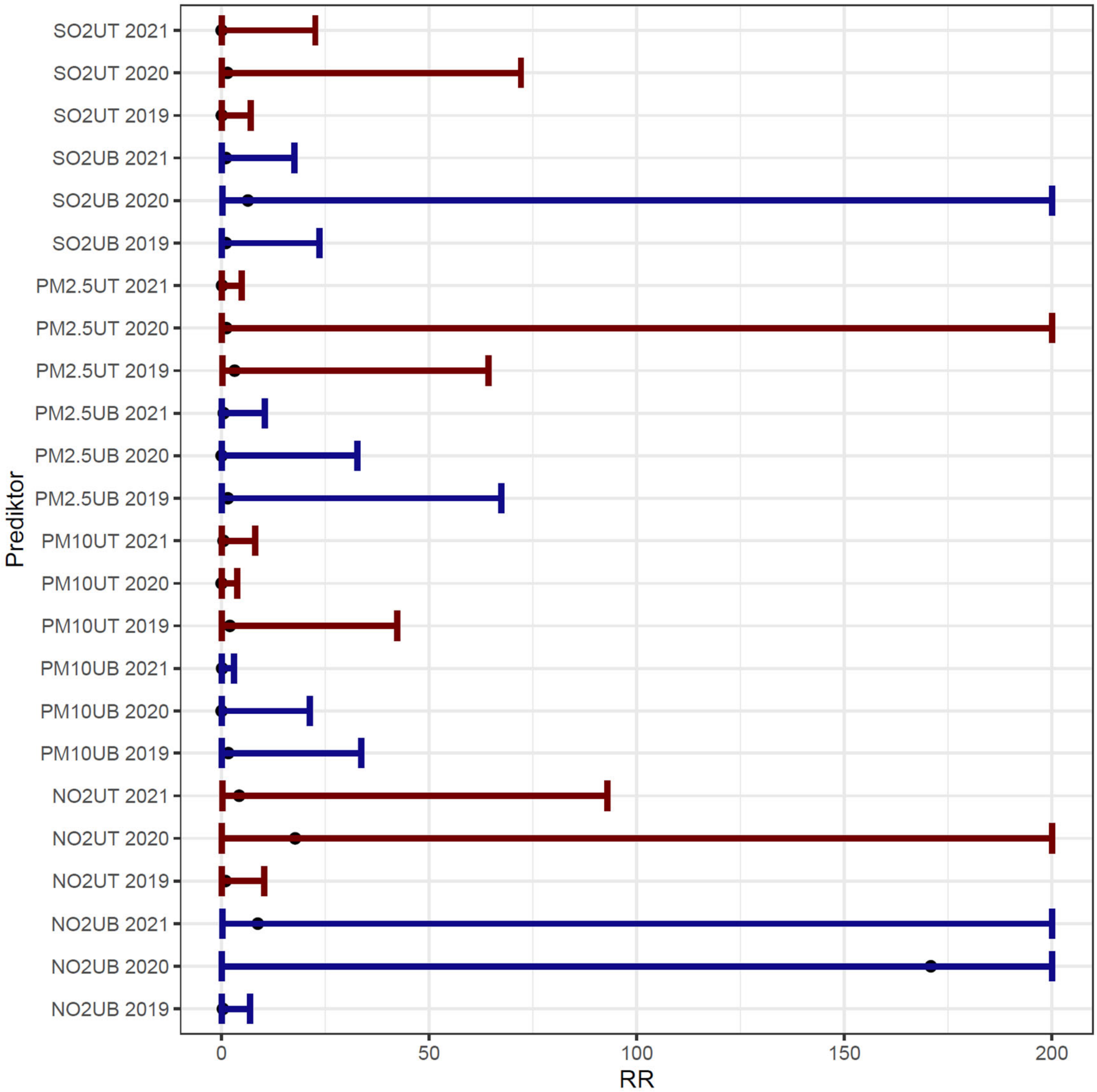

Figure 4. The influence of exposure to air pollution during the March–June period of different years on the relative risk of AECOPD hospitalizations. Legend: For each air pollutant examined, the calculated RR values (represented by dots) and 95% CI (represented by vertical lines) are given.

4. Discussion

Our research had two primary objectives: to determine whether there was a reduction in the concentration of air pollutants during the COVID-19 lockdown and to ascertain whether there was a change in the number of non-infectious AECOPD hospitalizations compared to the same period in the year before and the year after the COVID-19 lockdown.

The analysis of the results pointed out that the average daily concentrations of the majority of the air pollutants investigated were lower during the May–June 2020 period compared to the corresponding time in the previous year. The greatest effect was observed for gaseous air pollutants (51% reduction in SO_2(UB) concentrations and 42% reduction in NO_2(UT) concentrations). These results confirm the positive effects of COVID-19 lockdown on the reduction in air pollution emissions, mainly due to reduced traffic activity as a result of movement restrictions and increased remote work, along with decreased industrial and construction activities due to the closure or reduced capacity of many businesses. Furthermore, the average daily concentrations of $PM_{2.5}$ were even lower in 2021 compared to the same period in 2020. It is challenging to pinpoint the precise explanation for this, but a combination of complex associated effects of meteorological factors and air pollution, changes in emissions from diverse sources, technological advancements, and behavioral shifts among the general population (reminiscent of the long-term consequences of previous lockdown measures) could have contributed to the observed differences in $PM_{2.5}$ concentrations between the two periods.

In a recently published European Commission report on the environmental and climate status in the Western Balkan countries [22], the impact of the COVID-19 lockdown on air quality in other Serbian cities (Belgrade and Užice) was also analyzed. It was found that there was a reduction in the concentration of traffic-related air pollutants (NO and NO_2) by 50% to 80% (depending on the location of the monitoring station) compared to the same period from 2015 to 2019. During the initial months of the COVID-19 pandemic, air pollution levels decreased in almost all other regions of the world, with the greatest reductions observed in NO_2 emissions due to traffic restrictions. Muhammad et al. [23] determined that during the lockdown in Italy, Spain, France, and China, NO_2 emissions were reduced by 20–30%; in the United States, the emission of this gas was reduced by about a quarter compared to the historical average [24]; in Egypt, a reduction of 15–33% was observed compared to the five pre-pandemic years [6]; and in the United Kingdom, emissions of all nitrogen oxides from traffic have been reduced by 32–50% [25]. Considering the greater variety of emission sources, the decrease in particulate air pollution was somewhat lower but still significant [1], which is similar to our findings. Mexico City experienced a statistically significant decrease in particulate air pollution during the first year of the pandemic compared to 2019 [26], while in Palermo, Italy, PM_{10} concentrations decreased by 45% [27], and in Kazakhstan, the concentration of $PM_{2.5}$ decreased by 21% compared to the pre-lockdown period [28]. Analyzing the levels of air pollution during the lockdown in 278 Chinese cities, Yumin et al. [7] determined a drastic reduction in all observed environmental air pollutants, with the exception of ozone (on average, $PM_{2.5}$ concentrations decreased by 14.3 $\mu g/m^3$, PM_{10} by 22.2 $\mu g/m^3$, NO_2 by 17.7 $\mu g/m^3$, and SO_2 concentrations decreased by 2.9 $\mu g/m^3$).

In our study, there was a lower number of AECOPD hospitalizations during the COVID-19 lockdown compared to the same period of the previous and following years. A reduced number of AECOPD hospitalizations during COVID-19 lockdown was observed in several different Balkan countries, such as Greece [29] and Slovenia [30], as well as in several other countries across the globe—in Hong Kong [31], United Kingdom [32], and Singapore [33].

There are several potential explanations for these results. Firstly, the emergence of a new, previously unknown infectious disease imposed the need for reorganization of healthcare services worldwide, including in Serbia and the City of Novi Sad, redirecting a large portion of human and economic resources towards the care of COVID-19 patients. This also led to changes in the behavior of chronic patients, who avoided visits to healthcare facilities to reduce the objective risk of potential SARS-CoV-2 virus infection [34]. As a result, it is possible that some patients with mild exacerbations of COPD treated their symptoms at home without seeking help from healthcare institutions or managed their symptoms through remote communication with a doctor (telemedicine) [35]. Next, it is possible that there was indeed a decrease in the frequency of AECOPD in the initial stages of the pandemic, as the implementation of personal protective measures, such as wearing masks, frequent hand washing and disinfection, as well as adherence to social distancing measures, could have had an effect on preventing the transmission of other respiratory infectious agents that act as triggers for AECOPD, such as influenza viruses and RSV [32,33]. It has also been hypothesized that patients had higher adherence to prescribed inhalation therapy [34] and that they quit smoking or reduced the number of cigarettes smoked per day due to fear of exacerbating their underlying condition in pandemic conditions [32]. Another potential explanation for the reduced number of AECOPD cases during the initial months of the COVID-19 pandemic is the under-recognition and underdiagnosis of these conditions due to similar clinical manifestations [36], as well as increased mortality at home before patients sought medical attention or had the opportunity to receive medical assistance [37].

Due to the study's design, we were unable to analyze the effects of previously discussed factors on the frequency of AECOPD hospitalizations in our sample, but we did examine the impact of exposure to air pollution during COVID-19 lockdown on the risk of AECOPD hospitalization. After the implementation of "dlnm," no statistically significant difference was observed in the risk of hospitalization for AECOPD of non-infectious etiology when comparing the pre-pandemic period to the lockdown period, suggesting that exposure to reduced levels of air pollution did not result in a reduced number of severe AECOPD.

Although less available, there are studies that have examined the effect of air pollution reduction during the early stages of the COVID-19 pandemic on morbidity and mortality due to respiratory diseases. During the period of traffic restrictions, Irish researchers observed a statistically significant decrease in average annual NO_2 concentrations, which was associated with a decrease in hospitalizations for chronic respiratory diseases [38,39]. Similarly, a French study discovered that a 22% reduction in $PM_{2.5}$ emissions in 2020 was associated with a 3.2% reduction in pediatric physician visits due to worsening asthma symptoms, while a 32% reduction in NO_2 concentrations was associated with 1.5% fewer hospitalizations for respiratory diseases compared to the pre-pandemic period [40]. However, only a few studies have examined the impact of air pollution during the COVID-19 pandemic on AECOPD-related morbidity and mortality. According to a study from Iran, the number of AECOPD hospitalizations attributable to NO_2 exposure was 21% lower in 2020 than in 2019 under conditions of reduced air pollutant concentrations [41]. Another Iranian study established that the AECOPD-related mortality rate attributed to $PM_{2.5}$ in 2019 was 25.18%, while in 2020 it was 22.5% [42]. As a consequence of the reduction of NO_2 emissions during the lockdown, a study from China discovered that 920 AECOPD-related deaths were avoided [43]. Another case study from China found that a reduction in $PM_{2.5}$ emissions was associated with an 18% decrease in AECOPD-related premature mortality [44]. In the study by Ko et al. [45], it was determined that during the first year of the pandemic, there was a statistically significant decrease in the concentrations of PM_{10}, NO_2, and SO_2 compared to the three years preceding the pandemic, which contributed 3.8%, 4%, and 11%, respectively, to the reduction in AECOPD hospitalizations. A study from Greece found that exposure to NO_2, $PM_{2.5}$, and PM_{10} (but not SO_2 exposure) was positively associated with the average number of hospital admissions due to AECOPD in 2020, whereby this number decreased statistically significantly during the lockdown compared to the control pre-pandemic period, which the authors explained by the potential effects of reducing air pollution emissions as well as avoiding seeking medical care by elderly patients [46]. However, none of the mentioned studies used "dlnm" models in the statistical analysis, so it is difficult to compare such results with the results of our research. This also applies to the study by Chan et al. [31], in which, just like in ours, exposure to air pollution during the first three months of the pandemic did not have a statistically significant effect on the number of AECOPD hospitalizations.

There are several potential explanations for these results of our study, some of which represent the limitations of the study at the same time. Firstly, we analyzed only AECOPD hospitalizations of non-infectious etiology, thus excluding the potential interactions between air pollutants and infectious agents. Then, we observed a further decrease in the concentration of some air pollutants (such as $PM_{2.5}$(UB) and $PM_{2.5}$(UT)) in the year after the COVID-19 lockdown, which may have influenced the results as well. Furthermore, changes in meteorological conditions during the COVID-19 lockdown could have influenced the risk of non-infective AECOPD hospitalizations, regardless of the level of air pollution. It is also important to consider the lag effects of changes in air pollution levels and their impact on health outcomes. While short-term exposure to reduced air pollution levels may not immediately translate into a decrease in severe AECOPD cases (those requiring hospitalizations), sustained improvements in air quality may eventually lead to tangible health benefits. Furthermore, cumulative exposure to air pollutants over time may have lasting effects on respiratory health, making it challenging to observe immediate improvements in AECOPD hospitalization rates during a relatively short-term lockdown period. Finally, none of the previously referenced studies, including our own, included in the analysis individual exposure to indoor air pollution. Although in nearly all regions where the lockdown was implemented, the population's exposure to ambient air pollution decreased, little is known about the effects of exposure to air pollution within the indoor environments where individuals reside. Even though there are assumptions that measures implemented to prevent the spread of SARS-CoV-2 infection did not contribute to the reduction in indoor air pollution [26], one Chinese study that monitored $PM_{2.5}$ concentrations in 147 homes from 30 villages using special analyzers found that during the lockdown there was no statistically significant increase in the concentration of these particles compared to the period before the pandemic [47], whereas another Chinese study demonstrated that during the lockdown in China there was a significant increase in the $PM_{2.5}$ indoor concentrations [48]. Notwithstanding, considering the recommendation to stay indoors, it is plausible that the populace may have been subjected to prolonged exposure to certain levels of indoor air contaminants, rendering them vulnerable to the adverse consequences of air pollution. Other limitations of our study must be considered when interpreting the results, such as the small number of AECOPD hospitalizations originating from a single center, the inability to assess the actual individual exposure to air pollution, and the inability to control other variable factors that could affect individual exposure, such as housing conditions, air conditioning in patients' living spaces, time spent outdoors, wearing a face mask and applying other measures of personal protection, socio-economic living conditions, and so on.

5. Conclusions

In this study, there was a notable reduction in the concentrations of the majority of the selected air pollutants (particularly gaseous ones) during the COVID-19 lockdown compared to the same period in the pre-pandemic year. Despite the significantly lower number of hospitalizations for AECOPD during March–June of 2020 compared to the same period in 2019, exposure to reduced concentrations of ambient air pollutants during the COVID-19 lockdown did not lead to a statistically significant alteration in the relative risk of AECOPD hospitalizations stemming from non-infectious causes.

Undeterred by these findings and considering the previously given explanations of the results and the study's limitations, the positive effects of reducing air pollution emissions on human health cannot be underestimated, which is why public health initiatives should continue to focus on improving air quality. This entails primarily implementing stringent emission controls, promoting clean energy technologies, and encouraging sustainable transportation practices.

It is also important to acknowledge that short-term reductions in air pollution levels may not result in an immediate decrease in AECOPD hospitalization rates; thus, it is important to recognize the long-term benefits of environmental interventions aimed at reducing air pollution levels. Future longitudinal research tracking changes in air quality over time is essential for evaluating the effectiveness of air pollution reduction on AECOPD morbidity and guiding future policy decisions aimed at mitigating air pollution effects.

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Informed Consent Statement: Patient consent was waived due to the observational nature of the study.

Data Availability Statement: Publicly available data on air pollutant concentrations can be retrieved from the Serbian Environmental Protection Agency's website (http://www.sepa.gov.rs/ (accessed on 18 August 2022)). The data presented in this study are available upon request from the corresponding author.

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