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Original Research

Air Pollution and Hospital Admissions for Respiratory Diseases in Nis, Serbia

Ljiljana Stosic[1]*, Natasa Dragic[2], Dusica Stojanovic[1], Konstansa Lazarevic[3], Sanja Bijelovic[2], Marija Apostolovic[1]

[1]University of Nis, Faculty of Medicine, Dr Zorana Djindjica 81, 18000 Nis, Serbia
[2]University of Novi Sad, Faculty of Medicine, Hajduk Veljkova 3, 21000 Novi Sad, Serbia
[3]State University of Novi Pazar, Departmant of Biomedical sciences, Vuka Karadzica 9, 36300 Novi Pazar, Serbia

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Abstract

The study was aimed to investigate the effects of air pollutants particulate matter ($PM_{2.5,}$ PM_{10}), sulfur dioxide (SO_2) and NO_2 on hospital admissions for respiratory diseases in the residents of Nis, Serbia, during the period 2012-2014. The findings of average daily concentrations of air pollutants were obtained both by the measurements made by the Public Health Institute Nis and by the state ambient air quality monitoring network of the Agency for Environmental Protection of the Republic of Serbia. The respiratory diseases analyzed in the study are pneumonia, asthma, and chronic obstructive pulmonary disease (COPD). Patients were categorized into three age groups (0-17.9, 18-64.9 and >65). Poisson regression was used to examine the link between air pollutants and respiratory health outcome at lag 0. Results was expressed as the increase in Relative Risk (RR) for hospital admissions for each daily increase in air pollutants for 10 $\mu g/m^3$. NO_2 had the most significant effect on hospital admission, although its concentrations did not exceed the prescribed values. With an increase in the daily NO_2 concentrations of 10 $\mu g/m^3$, the RR of daily asthma and COPD hospital admissions in Nis older than 65 years increased by 1.2% and 0.7%, respectively. In women older than 65 years, with an increase in daily concentrations of NO_2 of 10 $\mu g/m^3$, the risk of daily hospital admissions for asthma increased by 1.5%. In multi-polluted statistical analysis (adjusted with $PM_{2.5}$ and SO_2) each daily increase in NO_2 for 10 $\mu g/m^3$ was statistically significant associated with the increased RR by 1.3%. In men 18 to 64 years of age, with an increase in daily NO_2 concentrations of 10 $\mu g/m^3$, the RR of hospital admissions for asthma increased by 2.0%, and in the $PM_{2.5}$-adjusted model, increased by 1.8%. The suspended particles had an effect on hospital admission for pneumonia in men up to 17.9 years of age. With an increase in daily concentrations of suspended $PM_{2,5}$ particles of 10 $\mu g/m^3$, the risk of hospital admissions for pneumonia in them increases by 0.6% and 0.4%, respectively. We found that the concentration of NO_2 even lower of national limit value had the greatest impact on hospital admission due to COPD in elderly

*e-mail: ljstosic@live.com

men and asthma in elderly women. Suspended particles had a significant effect on hospital admission for pneumonia in younger men.

Keywords: air pollutants, respiratory deseases, hospital admissions

Introduction

Ambient air pollution is considered to be one of the most important environmental risk factors for the public health. According to the World Health Organization report, around 4.2 million deaths worldwide are linked to exposure to air pollution [1]. Numerous epidemiological studies have shown the harmful health effects of air pollution, especially on the respiratory and cardiovascular systems [2-6].

In recent years, more attention has been given to particulate matters which, because of its size, presents a greater risk to the respiratory system. Exposure to particles of size 10 μm or less is associated with acute exacerbation of some respiratory diseases such as asthma, bronchitis, pneumonia, and chronic obstructive pulmonary disease (COPD) [7, 8]. However, there is no doubt that as well as particles, gaseous pollutants, dominantly nitrogen oxide (NO_2) could also have negative health effects. Some authors state that the negative effect of particles could be adjusted to the effect of NO_2, or vice versa, which means that it is very difficult to separate their effects [9].

Until now, for the territory of Nis, the results of ambient air quality monitoring showed that particulate matter (PM) presents the biggest problem. PM_{10} concentrations, especially in winter months, quite often exceed the values prescribed by current legislation (50μg/m^3). However, in this part of Serbia, no studies have been conducted on the impact of particulate matter on the health of the exposed population, while there is only a limited number of studies on the impact of gaseous air pollutants [10, 11].

The aim was to investigate the effects of air pollutants particulate matter ($PM_{2.5,}$ PM_{10}), sulfur dioxide (SO_2) and NO_2 on hospital admissions for respiratory diseases in the residents of Nis, Serbia, during the period 2012-2014.

Material and Methods

Study Area

The study was carried out in Nis. Nis is the third largest city in southeastern Serbia, with a population of over 250 000, and by air pollution among the most polluted cities in Serbia. It can be said that the numerous reasons contribute to the fact that Nis is one of the most polluted cities in Serbia. First of all, the city has a very unfavorable geographical position. Namely, it is located in a valley that is closed on three sides. Under the influence of the dominant, northwest wind, pollutants are distributed directly from the industrial zone to the urban area of the Nis basin. Although the industrial zone is not very developed, it can also affect the ambient air quality in the city. In Nis, the climate is moderately continental, with frequent temperature inversions that prevent vertical airflow. Temperature inversions are most common during the heat season, from October to March. It's over a hundred days a year with fog and haze [12]. Such conditions are likely to have a significant effect on increasing concentrations of air pollutants. According to the authors, almost two-thirds of the city's population are not connected to a district central heating system, but use their own individual heating method. The most significant sources of air pollution in the city are traffic and heating.

Environmental Data

The findings of average daily concentrations of PM_{10}, nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) from 2012 to 2014 were obtained both by the measurements made by the Public Health Institute Nis and by the state ambient air quality monitoring network of the Agency for Environmental Protection of the Republic of Serbia on the territory of the City of Nis. Through the investigation period, monitoring network for PM_{10} was covered by two stations, for NO_2 by three stations and for SO_2 also by the three stations.

The concentrations of $PM_{2.5}$ were obtained by mathematical calculation of multiplying the average daily values of PM_{10} by a coefficient of 0.67 [13]. Meteorological data for the study period were obtained from the Hydro-meteorological Institute of the Republic of Serbia, the station of the City of Nis, which is located in the Nis Fortress at 202 MAMSL [12]. The data included the daily average ambient temperature and daily average relative humidity based on synoptic observations.

Health Data

The data about daily hospital admission for respiratory diseases at the Clinical Center Nis were obtained by the Center for Informatics and Biostatistics in Public Health Institute Nis from 2012 to 2014. The data of hospital admissions was analyzed only for residents of the city of Nis. The data included the date of admission, the diagnostic code of the disease according to the International Classification of Diseases 10^{th} Revision (ICD-10) of each admission, and the age and gender of the patients. The respiratory diseases analyzed in the study are pneumonia (J12-J18), asthma

Table 1. Distribution of air pollution variables in Nis, Serbia, (2012-2014).

		Mean	SD	Min	Max	ANOVA F	ANOVA p
NO_2 (μg/m^3)	Spring	28.89	8.50	9.42	51.62	47.916	0.000
	Summer	25.76	7.45	8.33	51.11		
	Fall	29.24	12.28	7.72	93.57		
	Winter	36.32	13.27	13.27	89.01		
	Year	29.99	11.28	7.72	93.57		
SO_2 (μg/m^3)	Spring	6.65	4.23	1.80	27.90	116.563	0.000
	Summer	6.57	2.09	2.50	23.60		
	Fall	6.90	4.25	1.60	31.90		
	Winter	13.54	8.34	3.30	39.40		
	Year	8.38	5.97	1.60	39.40		
PM_{10} (μg/m^3)	Spring	28.23	14.55	6.15	87.05	129.241	0.000
	Summer	21.52	9.89	0.68	76.71		
	Fall	45.35	28.35	4.50	191.32		
	Winter	60.65	39.33	0.04	257.74		
	Year	38.67	29.75	0.04	257.74		
$PM_{2.5}$ (μg/m^3)	Spring	18.91	9.75	4.12	58.32	129.240	0.000
	Summer	14.42	6.63	0.46	51.40		
	Fall	30.38	18.99	3.02	128.18		
	Winter	40.63	26.35	0.03	172.69		
	Year	25.91	19.93	0.03	172.69		

(J45-J46), and chronic obstructive pulmonary disease (COPD) (J44). Patients were categorized into three age groups: the first group aged 0-17.9, the second 18-64.9 and third group >65, in order to assess the relative incidence of respiratory illnesses in relation to age.

Statistical Analyses

For the purpose of this paper, basic descriptive statistical analysis was used for environmental and health data (average, minimum, maximum, standard deviation, frequency distribution). Pearson correlation coefficient was used to examine the correlation among all environmental variables. Yearly and season variation among air pollutants was determined by ANOVA. Poisson regression was used to examine the link between air pollutants and respiratory health outcome at lag 0. At the beginning for each respiratory outcome, a core model was built by day of the study (linear term), year, month, season (spring, summer, autumn, winter) and temperature (quadratic term) as well as relative humidity (linear term) [14]. The final model was chosen according to the Akaike's Information Criteria (AIC) and lack of overdispersion or under dispersion. If it was necessary, each model was reviewed by negative binomial regression in order to check the influence of overdispersion on the results. Each air pollutant was separately included in the model and if link was significant, then multi-pollution regression model was run. Because of the multicollinearity of the PM_{10} and $PM_{2.5}$ they were always included separately in each regression model. Results was expressed as increase in Relative Risk (RR) for hospital admissions for each daily increase in air pollutants for 10 μg/m^3. The level of p value <0.05 was considered as statistically significant. For all statistical analysis SPSS software, version 21 was used.

Results

During the study period between 2012-2014, the mean daily concentrations of NO_2, SO_2, PM_{10} and $PM_{2.5}$ were 29.99 μg/m^3±11.28, 8.38 μg/m^3±5.97, 38.67 μg/m^3±29.75 and 25.91 μg/m^3±19.93, respectively. The highest average values were detected during the winter. Some significant differences in the concentrations of all air pollutants were found by season (Table 1).

Table 2. Concentrations of air pollution variables in Nis, Serbia, (2012-2014).

		N	Mean	SD	Min	Max	ANOVA	
							F	p
NO_2 (µg/m^3)	2012	366	30.88	9.74	14.16	74.51	2.209	0.110
	2013	365	29.98	12.36	8.33	93.57		
	2014	365	29.13	11.54	7.72	89.01		
	Total	1096	29.99	11.28	7.72	93.57		
SO_2 (µg/m^3)	2012	366	12.49	7.87	4.20	39.40	178.801	0.000
	2013	365	5.65	3.36	1.60	23.00		
	2014	365	6.98	2.75	3.40	24.70		
	Total	1096	8.38	5.97	1.60	39.40		
PM_{10} (µg/m^3)	2012	366	44.02	30.10	0.04	257.74	12.717	0.000
	2013	365	33.04	31.74	0.68	191.30		
	2014	365	38.92	26.19	10.10	196.22		
	Total	1096	38.67	29.75	0.04	257.74		
$PM_{2.5}$ (µg/m^3)	2012	366	29.49	20.17	0.03	172.69	12.717	0.000
	2013	365	22.14	21.26	0.46	128.17		
	2014	365	26.08	17.55	6.77	131.47		
	Total	1096	25.91	19.93	0.03	172.69		

Average annual NO_2 concentrations did not differ significantly by year (p = 0.110), in contrast to average annual SO_2, PM_{10} and $PM_{2.}$ concentrations, which were highest in 2012 (Table 2).

The average air temperature in the study period, was 13.13ºC±8.95ºC and the average relative humidity was 67.77%±14.08% (Table 3).

Pearson correlation for the selected variables showed positive correlation between all air pollutants (p<0.01). The strongest positive correlation was observed between NO_2 and PM particles (r = 0.474; p = 0.000). The statistical significant (p<0.01) negative correlation was observed between air temperature and all air pollutants. Air humidity was positively correlated with SO_2 and PM particles (PM_{10} and $PM_{2.5}$) and negatively correlated with NO_2. Some higher significance was found between air humidity and PM particles. The strongest statistical significant negative correlation was between air temperature and air humidity (Table 4).

During the study period, a total of 6205 patients were admitted to the hospital for respiratory diseases that have been observed (pneumonia, COPD and asthma). In relation to gender and group of respiratory diseases, each year the number of admissions for pneumonia and COPD were higher among men, while admissions for asthma were most frequent among women (Table 5).

The highest average number of hospital admissions was for COPD, in persons over 65 years of age and

Table 3. Distribution of meteorological parameters (temperature and relative humidity) in Nis, Serbia, (2012-2014).

		Min	Max	Mean	Median	SD
Temperature (ºC)	Spring	5.86	29.2	16.51	16.5	5.86
	Summer	11.5	30.5	22.67	22.7	3.83
	Fall	-10.4	25.8	9.74	19.75	6.49
	Winter	-12.3	14.9	3.56	4.1	5.56
	Year	-12.3	30.5	13.13	13.5	8.95
Relative humidity (%)	Spring	36	99	63.07	60	14.47
	Summer	30	90	58.08	58	13.76
	Fall	41	96	74.35	75	10.49
	Winter	41	98	73.61	74	11.16
	Year	30	99	67.72	65	14.08

Table 4. Correlation between air pollutants and meteorological data.

		NO_2 (average)	SO_2 (average)	PM_{10} (average)	$PM_{2.5}$ (average)	Temperature (average)	Relative humidity (average)
NO_2 (average)	Pearson Correlation	1					
SO_2 (average)	Pearson Correlation	0.297**	1				
PM_{10} (average)	Pearson Correlation	0.474**	0.370**	1			
$PM_{2.5}$ (average)	Pearson Correlation	0.474**	0.370**	1.000**	1		
Temperature (average)	Pearson Correlation	-0.239**	-0.463**	-0.453**	-0.453**	1	
Relative humidity (average)	Pearson Correlation	-0.039	0.094**	0.224**	0.224**	-0.621**	1

** correlation is significant at the level p<0.01

Table 5. The number of total hospital admissions and by gender in the period 2012-2014.

Diseases/Y	2012		2013		2014		Total	
	Male	Female	Male	Female	Male	Female	Male	Female
Pneumonia	278	258	257	215	219	166	754	639
COPD	951	507	530	250	471	235	1952	992
Asthma	328	423	272	419	178	248	778	1090
Total	2 745		1 943		1 517		6 205	

ages 18 to 65 (1.58±2.25 and 1.05±1.65, respectively). A slightly lower number of hospital admissions, related to asthma and pneumonia admissions, were in patients aged 0 to 18 years (0.78±1.65 and 0.53±0.99, respectively) (Table 6).

Considering the impact of each pollutant separately, it has been found that NO_2 contributes to the increase in hospital admissions for asthma and COPD in people over 65 years of age (Table 7). During the study period, with an increase in daily NO_2 concentrations of 10 μg/m³, the RR of daily asthma and COPD hospital admissions in Nis of the residents over 65 years of age increased by 1.2% (95%CI:1.003-1.022) and 0.7% (95%CI:1.00-1.015), respectively. In adjusted model with $PM_{2.5}$ particles, the link between NO_2 and hospital admissions for asthmatic patients in Nis was the same. On the other hand, in adjusted model with SO_2 the relation between NO_2 and hospital admissions for COPD in residents of Nis, who are over 65, was more significant and slightly changed (RR-0.8%, 95% CI:1.000-1.015) (Table 7).

In women, older than 65, with an increase in daily concentrations of NO_2 of 10 μg/m³, the risk of daily hospital admissions for asthma increased by 1.5% (95% CI:1.003-1.027). In a SO_2-adjusted model, with

Table 6. Daily frequency of hospital admissions by age and group of respiratory diseases.

Diseases (age)	Min	Max	Mean	SD
Pneumonia (to 17.9)	0.00	11.00	0.53	0.99
Pneumonia (18 to 64.9)	0.00	7.00	0.44	0.80
Pneumonia (over 65)	0.00	5.00	0.30	0.65
COPD (to 17.9)	0.00	2.00	0.06	0.25
COPD (18 to 64.9)	0.00	17.00	1.05	1.65
COPD (over 65)	0.00	26.00	1.58	2.25
Asthma (to 17.9)	0.00	21.00	0.78	1.65
Asthma (18 to 64.9)	0.00	8.00	0.55	0.97
Asthma (over 65)	0.00	5.00	0.37	0.77

Table 7. Association between air pollutants and respiratory hospital admissions with 95% CI for increases of RR with daily 10μg/m^3 increases in air pollutants concentration.

	β	p	95% CI Exp(β)		
			Exp(β)	**Lower Bound**	**Upper Bound**
ASTHMA					
All>65 y					
NO_2	0.012	0.012	1.012	1.003	1.022
NO2 adjusted with $PM_{2.5}$	0.012	0.020	1.012	1.002	1.023
Male 18-64 y					
NO_2	0.020	0.010	1.020	1.005	1.035
NO2 adjusted with $PM_{2.5}$	0.018	0.033	1.018	1.001	1.034
NO2 adjusted with $PM_{2.5}$ & SO_2	0.018	0.029	1.018	1.002	1.035
Female>65 y					
NO_2	0.015	0.013	1.015	1.003	1.027
NO_2 adjusted with SO_2	0.015	0.010	1.016	1.004	1.028
NO_2 adjusted with PM_{10} & SO_2	0.013	0.042	1.013	1.000	1.026
NO_2 adjusted with $PM_{2.5}$	0.012	0.052	1.013	1.000	1.025
$PM_{2.5}$	0.009	0.054	1.009	1.000	1.019
PM_{10}	0.006	0.054	1.006	1.000	1.013
COPD					
All>65 y					
NO_2	0.007	0.057	1.007	1.000	1.015
NO_2 adjusted with SO_2	0.008	0.041	1.008	1.000	1.015
PNEUMONIA					
Male <18 y					
$PM_{2.5}$	0.006	0.037	1.006	1.000	1.012
$PM_{2.5}$ adjusted with NO_2	0.006	0.049	1.006	1.000	1.012
$PM_{2.5}$ adjusted with SO_2	0.006	0.031	1.006	1.000	1.012
$PM_{2.5}$ adjusted with NO_2 & SO_2	0.006	0.045	1.006	1.000	1.012
PM_{10}	0.004	0.037	1.004	1.000	1.008
PM_{10} adjusted with NO_2	0.004	0.049	1.004	1.000	1.008
PM_{10} adjusted with SO_2	0.004	0.031	1.004	1.000	1.008
PM_{10} adjusted with NO_2 & SO_2	0.004	0.045	1.004	1.000	1.008

Table contains only results for statistical significance association

an increase in daily concentrations of NO_2 of 10 μg/m^3, the risk of hospital admissions for asthma in women older than 65 increased by 1.6% (95%CI:1.004-1.028), while in the adjusted model with $PM_{2.5}$ particles increased by 1.3% (95%CI:1.000-1.025), but within the limit of statistical significance (p = 0.052). In multi-polluted statistical analysis (adjusted with $PM_{2.5}$ and SO_2) each daily increase in NO_2 for 10μg/m^3 was statistically significant when associated with the increased RR by 1.3% (95%CI:1.000-1.026).

The suspended particles, in a single polluted model, had a marginally significant impact on hospital admission for asthma in women older than 65 years. Namely, with an increase in daily concentrations of suspended $PM_{2.5}$ and PM_{10} particles of 10 μg/m^3, the RR increased by 0.9% (95% CI:1.000-1.019) and 0.6% (95%CI:1.000-1.013), respectively (p = 0.054).

In men, 18 to 64 years of age, with an increase in daily NO_2 concentrations of 10μg/m^3, the RR of hospital admissions for asthma increased by 2.0% (95%CI:1.005-

1.035), and in the $PM_{2.5}$-adjusted model, it increased by 1.8% (95%CI:1.001-1.034).

The suspended particles had an effect on hospital admission for pneumonia in men up to 17.9 years of age. With an increase in daily concentrations of suspended $PM_{2,5}$ particles of 10 μg/m^3, the risk of hospital admissions for pneumonia in them increased by 0.6% (95%CI:1.000-1.012) and 0.4% (95%CI:1.000-1.008), respectively. This percentage of increasing RR for hospital admissions for suspended particles does not change in models where the control of other pollutants (NO_2 and SO_2) was done.

Discussion

The results of our study showed that the values of NO_2 and SO_2 were within the limits, by national regulations, of the prescribed values. As for the values of particles (PM_{10} and $PM_{2.5}$), they were significantly higher than prescribed. The maximum recorded values of PM_{10} and $PM_{2.5}$ were 257.4μg/m^3 and 172.7 μg/m^3, respectively. The average daily concentrations of NO_2, SO_2, PM_{10} and $PM_{2.5}$ in the examined period did not differ significantly from the concentrations of previous years. Air quality in Nis, mainly due to high values of PM particles is often classified in category III (excessively polluted air) [15]. It can be said that the numerous reasons (unfavorable geographical position, frequent temperature inversions, individual way of heating) contribute to the fact that Nis is one of the most polluted cities in Serbia. Our study also showed that NO_2, SO_2 and PM particles concentrations were significantly higher during the heating season. The worst effect of the heating season is reflected in a significant increase in the concentration of particles, while the concentrations of NO_2 and SO_2 were slightly increased in the heating season. This result was to some extent expected because the main source of particles pollutants is primarily fosil fules (heating) and traffic, while for NO_2-it is traffic, which is constantly present, without such strong seasonal differences. Many studies have also found higher concentrations of pollutants in the air during heating seasons and by 70% [16-18].

In our study, the concentrations of all monitored air pollutants were positively correlated suggesting that they could have a similar source type. Matching the results of the seasonal variations and correlation among air pollutants, it could be that the two leading sources of air pollution colud be heating and traffic. Meteorological factors also have a significant influence on the concentrations of pollutants in the air [19], which was confirmed by our research. Thus, a statistically significant negative correlation that was found between air temperature and all air pollutants, confirmed the previous results of seasonal variation and influence of heating season. A higher significance was found between air humidity and PM particles. Knowing that a part of the $PM_{2.5}$ particles in the air could be seen as secondary pollutants and that a chemical reaction leading to the $PM_{2.5}$ could be highly influencing the air humidity, these results of correlation were expecetd. However, in contrast to our study, some other results have shown that with decreasing air humidity, the concentrations of suspended particles increase [20].

This study has confirmed that air pollutants were positively associated with hospital admissions for respiratory diseases. The highest number of hospital admissions was in 2012, when the highest values of air pollutants were recorded. COPD in persons over 65 years of age and ages 18 to 65 was the most common reason for hospitalization. A slightly lower number of hospital admissions related to asthma and pneumonia admissions were in patients aged 0 to 18 years. The number of admissions for pneumonia and COPD were higher among males, while admissions for asthma were most frequent among females.

It is interesting that the significant effect on hospital admission for respiratory diseases in our study had NO_2, although its concentrations did not exceed the prescribed values. This practically means that these lower concentrations are also significant, especially in the more sensitive part of the population (elderly people). The WHO also suggested that there are no safe levels for air pollutants [21] and there is no threshold in the health effects of air pollution at the population level. In our research, it was found that NO_2 in people older than 65 years contributes to the increase in hospital admissions for asthma and COPD. The risk of daily asthma and COPD hospital admissions of residents over 65 years of age in Nis increased by 1.2% and 0.7%, respectively. NO_2 is considered as a key precursor for a range of secondary pollutants. In combination with the other pollutants, its effect on the health of those exposed is likely to increase. Small deviations in NO_2 concentrations per season, that we discovered in this study, are an indirect proof that the main source of this pollutant is primarily traffic. Its permanent presence in the air throughout the year, even in a lower concentration, poses a danger to the health of the elderly in particular.

An ecological study in Spain showed that hospital admissions for COPD were positively correlated with increased atmospheric concentrations of NO_2, PM_{10} and SO_2 [22]. Similar results were found in a study in Bangkok in which an increase of 10 μg/m^3 in NO_2, SO_2 and PM_{10} at lag 0-1 day was associated with an increase in hospital admissions for respiratory diseases by 1.42%, 4.49% and 1.18%, respectively [6] and in a study in Vietnam [23]. A study by a group of authors in Beijing, China about the effects of air pollutants on COPD, showed that cumulative lag effect with per 10μg/m^3 increase in air pollutants was the largest for nitrogen dioxide (NO_2) with 3.03% at lag 06, for sulfur dioxide (SO_2) with 2.07% at lag 01, for PM_{10} with 0.92% at lag 07, and for $PM_{2.5}$ with 0.82 % at lag 06 [24]. They also found that larger risk effect was in males and the elderly. Our research did not follow the delayed effect of air pollutants on hospital admission for respiratory diseases. In our opinion, if there is a longer delayed effect, lag 06 for example, the question arises whether air pollution is decisive, ie the only factor that affects hospital admission. However, our future research should follow the delayed effect of air pollutants.

COPD is characterized by a restriction of airflow in the airways. Air flow limitation is progressive and associated with inflammatory response of the lungs to harmful particles or gases [25]. In addition to smoking and genetics, the development of COPD can also be affected by air pollution. NO_2 exhibits a broncoconstrictive effect, which causes an additional decrease in expiratory volume, to which elderly patients with a pre-existing diagnosis of COPD are particularly sensitive [26]. In contrast to these results, a group of authors in Novi Sad, Serbia, did not find a significant association between NO_2 and hospital admission due to COPD [27]. In an adjusted model with $PM_{2.5}$ particles RR for hospital admissions for asthma in residents of Nis who are over 65, and is related to NO_2 increase, was the same, suggesting that modifying the effects of $PM_{2.5}$ is not so important for the health effects of NO_2, but nonetheless incresed the uncertainty of RR for NO_2 according to the increased of p value.

In our study NO_2 had a significant effect on hospital admission for asthma im men aged 18 to 64 and in women older than 65, both alone and in adjusted models with other pollutants. Asthma is affecting over 334 million people around the world [17, 19]. There are consistent findings which indicate that ambient air pollutants (both gaseous and suspended particles) play an important role in the exacerbation of asthma [28]. Each of the air pollutants has a special mechanism of effect. NO_2 causes lipid peroxidation of the cell membrane and the formation of free radicals that impair the structure and function of the airways. Exposure to nitrogen dioxide can accelerate the release of inflammatory mediators [29]. SO_2, an inorganic chemical irritant, is known to cause airway inflammation, eosinophilia, bronchospasm and airway fibrosis in asthma [30]. Particle matters have a more complex effect on asthmatic airways as their deposition in the airways directly causes inflammation, mucosal edema and cytotoxicity [31]. However, slight changes in RR for NO_2 and asthma in the multipolluted model in our study revealed that NO_2 was the leading cause of hospital admission, while there was also a small impact of other analyzed air pollutants, meaning that the impact of NO_2 was not separate from the others pollutants.

In our study, the suspended particles also had a borderline significant impact on hospital admission for asthma in women aged over 65. The higher number of women who experienced asthma problems may be due to their increased exposure to suspended particles indoors (cooking on wood stoves). Gender differences can also be a consequence of hormonal status, exposure at work, smoking, different reactions to stress [32]. Research in Beirut also has shown a significant impact of suspended particles. Thus, for each increase in suspended particulates by 10 $\mu g/m^3$, the RR for hospital admissions increased by 1.2% for PM_{10} and 1.6% for $PM_{2.5}$ [33]. Similar results were obtained in a study conducted in Istanbul, [34]. A study by a group of scientists found that $PM_{2.5}$, NO_2 and PM_{10} had the largest effects on asthma hospital admissions, though in children (0-17 years) [2]. The differences in the gathered results were probably a consequence of different chemical compositions of the particles, as well as of different climatic factors. Namely, it has been determined that the chemical composition of particles can also be influenced by meteorological factors [7].

In our study, the suspended particles had an effect on hospital admissions for pneumonia in male children up to 17.9 years of age. With an increase in daily concentrations of suspended $PM_{2.5}$ and PM_{10} particles of 10$\mu g/m^3$, the risk of hospital admissions for pneumonia in them increased by 0.6% and 0.4%, respectively. Results of the other studies showed that pneumonia, as an inflammatory condition of the lungs caused by infections, can be triggered and exacerbated by exposure to PM particles [35, 36]. The particles cause oxidative stress and inflammation which can weaken the cellular defenses and the immune system and increase susceptibility to bacterial pathogens. Due to the more pronounced oxidative potential of suspended particles in relation to gaseous pollutants such as NO_2 and SO_2, the effect on pneumonia was somewhat expected. It was probably also influenced by the composition of the particles, predominantly biological (viruses, bacteria, ie their fragments), considering that in our research we did not separate the specific from non-specific types of pneumonia. Otherwise, particles formed in the soil and in abrasive mechanical processes can also carry biological materials such as bacteria, mold or pollen and are likely to create additional harmful health effects in the respiratory system [37].

A study by a group of authors from Hong Kong also showed that increasing concentrations of PM particles affect a higher number of hospital admissions for pneumonia [36]. They found that women, the elderly and children were the ones most sensitive to the harmful effects of the particles. Children were also the most vulnerable group in the study in Lanzhou, China [38]. In contrast to ours, where male children were more sensitive, in the study in Lanzhou, female children were more sensitive. It is generally assumed that children are more sensitive to air pollutants than the elderly. They breathe a much larger amount of air per kilogram of body weight, thus entering a larger amount of pollutants into the body, have narrower airways and spend more time in various outdoor activities [39].

This is the first study to investigate the effects of ambient particulate matter and other gaseous pollutants (NO_2 and SO_2) on hospital admissions for respiratory diseases in this part of Serbia, but there are certain limiting factors. We did not monitor the delayed effect of pollutants or the seasonal nature of hospital admissions. Personal exposure in this study was determined based on the average daily concentration of aero pollutants. Other confounders, such as smoking, occupation, time spent outdoors, and socioeconomic status, were not included in this study.

Conclusion

In conclusion, we found that the concentration of NO_2 even lower of national limit value had the greatest impact on hospital admission due to COPD in elderly men and asthma in elderly women. Suspended particles had a significant effect on hospital admission for pneumonia in younger men. These results indicated and confirmed that continuous exposure to a lower concentration could be a more serious factor with the respiratory health effects among elderly, than the higher, but more variable concentration of particles throughout the investigated period.

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Conflict of Interest

The authors declare that no conflicts of interest exist.

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