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CORRELATION BETWEEN OCCURRENCE AND DETERIORATION OF RESPIRATORY DISEASES AND AIR POLLUTION WITHIN THE LEGALLY PERMISSIBLE LIMITS

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SUMMARY – The aim of the study was to investigate the unknown effect of air pollutants on the occurrence or deterioration of respiratory diseases in the area with a humid continental climate. This retrospective study included 5868 patients with respiratory symptomatology (upper respiratory tract infection (URTI), pneumonia, acute bronchitis, chronic obstructive pulmonary disease (COPD), and asthma) admitted to emergency department (ED). The number of patients, values of meteorological parameters (mean daily values of air temperature, pressure and relative humidity) and concentrations of air pollution particles (≤10 μm (PM_{10}), ozone (O_3) and nitrogen dioxide (NO_2)) were collected during a two-year (July 2008 – June 2010) period. There were 1839 (31.3%), 1712 (29.2%), 1313 (22.4%), 614 (10.5%) and 390 (6.6%) patients with pneumonia, COPD, URTI, acute bronchitis and asthma, respectively. The mean daily concentrations of NO_2 (25.9 (1.7-89.7) μg/m^3), O_3 (47.1 (4.7-135.4) μg/m^3) and PM_{10} particles (25.7 (4.6-146.6) μg/m^3) were below the legally defined thresholds. Among other results, the occurrence of respiratory diseases showed positive Spearman's correlation with the values of air humidity (days 0-3, r=0.15 to 0.19), PM_{10} (days 0-3, r=0.10 to 0.13) and NO_2 concentrations (day 0, r=0.11), and negative correlation with the values of air temperature (days 0-3, r=-0.36 to -0.34), pressure (day 0, r=-0.10) and O_3 concentrations (days 0-3, r=-0.21 to -0.22) ($p<0.05$ all). In conclusion, the occurrence of respiratory diseases showed correlation with weather conditions and air pollutants despite the legally permitted values in the region with a humid continental climate.

Key words: *Air pollution – adverse effects; Respiration disorders; Ozone; Nitrogen dioxide; Croatia*

Introduction

Climate changes, which according to recent data have a worsening trend, pose great threat to respiratory health by directly promoting or aggravating respiratory diseases or through the increasing exposure to risk factors for respiratory diseases[1]. Climate change increase the amount of pollen and allergen produced by each plant, mould proliferation, and the concentrations of outdoor ozone (O_3) and particulate matter (PM) at the ground level. The main diseases of concern are asthma, rhinosinusitis, chronic obstructive pulmonary disease (COPD) and respiratory tract infections

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(RTI). Groups at a higher risk of climate change effects include individuals with pre-existing cardiopulmonary diseases or disadvantaged individuals. Adaptation and mitigation measures are strongly needed[1].

The exposure to air pollutants and changes of meteorological parameters (air temperature, humidity and pressure) may be related to higher morbidity and mortality, as well as to a higher number of patients presenting to emergency department (ED)[2-4]. Air pollution poses great health risk even in developed countries with legally defined thresholds of air pollutant concentration[5,6].

Zagreb is the capital and the largest city (790,017 citizens, area 641 km^2) of the Republic of Croatia, a country situated in southeastern Europe[7]. The climate of Zagreb is classified as a humid continental. The average daily temperature in winter is around +1 °C (from December to February) and the average temperature in summer is 22.0 °C.

In this study, we investigated whether PM particles sized ≤10 micrometers (PM_{10}), nitrogen dioxide (NO_2) and O_3, as well as certain meteorological conditions had impact on ED visits of patients with various respiratory diseases in our area with a humid continental climate.

Subjects and Methods

This retrospective study included 5868 consecutive patients admitted to ED (Sestre milosrdnice University Hospital Center and Sveti Duh University Hospital) during a two-year period (June 2008 – July 2010). All patients were Zagreb residents. Information on daily ED visits were collected retrospectively from the information systems of the two hospitals. The study was approved by the institutional Ethics Committee. Given the observational design of the study, informed consent was waived. According to clinical presentation, radiology and laboratory findings, patients were classified into five groups, as follows: pneumonia, acute bronchitis, COPD, asthma, and upper respiratory tract infection (URTI). The concentrations of NO_2, O_3 and PM_{10} particles were collected by the National Monitoring Station Zagreb -1 (Environmental Protection Agency). The mean daily values of air temperature (°C), pressure (kPa) and relative humidity (%) were collected by the Meteorological and Hydrological Service of Croatia.

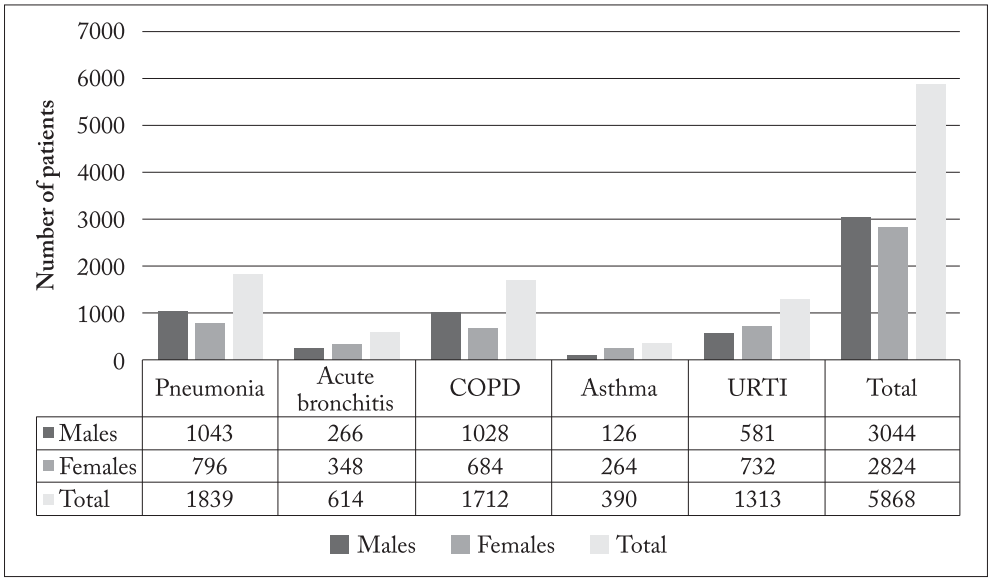
Statistical analysis

Qualitative data were expressed as absolute number and percentage. We used χ^2-test with Yates correction for analysis. Quantitative data were expressed as median and range. Differences between two and among three or more groups were tested by Mann-Whitney U-test and Kruskal-Wallis ANOVA test, respectively. Correlation between the number of patients with respiratory symptomatology, values of meteorological parameters and concentrations of air pollutants was assessed by nonparametric Spearman's correlation test. It was classified by Spearman's *r* value as very weak (0-0.19), weak (0.20-0.39), moderate (0.40-0.59), strong (0.60-0.79), and very strong (0.80-1.0) correlation. This guide also applied to negative correlations. The level of statistical significance was set at $p<0.05$. Processing was done using the STATISTICA 6.0 for Windows software.

Results

Of the total of 5868 patients, there were 1839 (31.3%), 1712 (29.2%), 1313 (22.4%), 614 (10.5%) and 390 (6.6%) patients with pneumonia, COPD, URTI, acute bronchitis and asthma, respectively (Fig. 1). We recorded the following results:

1. The occurrence of acute bronchitis, asthma and URTI was higher in females, and of pneumonia and COPD in males (Fig. 1). Age differences between males and females according to type of respiratory disease are presented in Table 1. Females with pneumonia, acute bronchitis, COPD and asthma were significantly older ($p<0.05$).
2. During the study period, the mean daily values of NO_2 (25.9 (1.7-89.7) μg/m^3) O_3 (47.1 (4.7-135.4) μg/m^3) and PM_{10} (25.7 (4.6-146.6) μg/m^3) were below the legally defined thresholds. Regarding the humid continental climate characteristics, the given mean daily values of air temperature (13.4 (-7.9-28.5) °C), relative humidity (68.9 (37.7-95.3) %) and air pressure (996 (966-1020) hPa) were expected.
3. Spearman's correlation analysis yielded the following significant results (Tables 2 and 3):
   a. total number of patients with respiratory symptomatology correlated with higher values of air humidity (days 0-3), PM_{10} (days 0-3) and NO_2 (day 0) concentrations, and



	Pneumonia	Acute bronchitis	COPD	Asthma	URTI	Total
Males	1043	266	1028	126	581	3044
Females	796	348	684	264	732	2824
Total	1839	614	1712	390	1313	5868

COPD = chronic obstructive pulmonary disease; URTI = upper respiratory tract infection

Fig. 1. Number of patients with respiratory diseases (pneumonia, acute bronchitis, COPD, asthma and URTI) admitted to emergency department during a two-year period (July 2008 – June 2010).

with lower values of air temperature (days 0-3), pressure (day 0) and O_3 concentration (days 0-3);

b. the occurrence of pneumonia correlated with higher values of air humidity, PM_{10} and NO_2 concentrations (days 0 and 1), and with lower values of air temperature (days 0-3) and O_3 concentration (days 0 and 1);
c. the number of patients with acute bronchitis correlated with higher values of air humidity (days 0-3) and PM_{10} concentration (days 2 and 3), and with lower values of air temperature and O_3 concentration (days 0-3);
d. the occurrence of COPD correlated with higher values of air humidity (days 0-3) and PM_{10} concentration (day 1), and with lower values of air temperature (days 0-3), air pressure (days 0 and 1) and O_3 concentration (days 0-3);
e. the occurrence of asthma correlated with higher and lower values of O_3 (days 0 and 3) and PM_{10} (days 0 and 2) concentrations, respectively; and
f. the occurrence of URTI correlated with higher values of air humidity (days 0-3) and PM_{10} concentration (days 0-2), and with lower values of air temperature (days 0-3), air pressure (day 0) and O_3 concentration (days 0-3).

Discussion

As already mentioned, this study investigated the impact of air pollutants and weather conditions on the occurrence of respiratory diseases in the area with a humid continental climate. It is important to emphasize that during the study period, daily concentrations of air pollutants were below the legally permissible upper limits.

In our study, the number of patients with respiratory diseases (except for asthma) correlated with higher and lower values of air humidity and temperature, respectively. Also, the number of patients with COPD correlated with lower air pressure. Cold temperature and low humidity were associated with increased occurrence of RTI[8]. Both of these conditions favor the spread of some viruses such as influenza virus[9-11], which through positive correlation with changes in the host physiological susceptibility, immune function, and behavioral patterns (cross-infection from indoor crowd-

Table 1. Age differences between males and females according to type of respiratory disease

Diagnosis	Male (median and range)	Female (median and range)	Mann--Whitney U test
Pneumonia	69 (17-97)	74 (16-99)	p<0.001
Acute bronchitis	52 (15-91)	60 (18-96)	p<0.001
COPD	74 (20-93)	76 (17-100)	P<0.001
Asthma	36 (15-88)	49 (15-86)	**p=0.005**
URTI	43 (14-92)	42 (13-98)	p=0.265
Kruskal-Wallis ANOVA	p<0.001	p<0.001	

COPD = chronic obstructive pulmonary disease; URTI = upper respiratory tract infection

ing) results in a higher rate of RTI. Other authors report on positive and negative RTI correlation with air humidity and temperature[12]. The higher incidence of COPD and asthma exacerbations during the periods of cold temperature has important consequences for patients in terms of increased morbidity and mortality[13-15]. It could be due to the increased prevalence of viral RTI circulating in cold conditions. In addition, other meteorological conditions such as high atmospheric pressure and low humidity can directly induce asthma and COPD[15-17].

Primary pollutants (e.g., nitrogen dioxide, NO_2) are released directly into the atmosphere, whereas secondary pollutants (e.g., ozone, O_3) result from chemical reactions among them. The most extensively studied pollutant is PM, which can be primary or second-

Table 2. Correlations between meteorological parameters and occurrence of respiratory diseases (July 2008 – June 2010)

	Days	Pneumonia		Acute bronchitis		COPD		Asthma		URTI		Total	
		r	p	*r*	p	*r*	p	*r*	p	*r*	p	*r*	p
Temperature (day 0)	730	-0.15	**<0.001**	-0.23	**<0.001**	-0.26	**<0.001**	0.06	0.119	-0.18	**<0.001**	-0.34	**<0.001**
Temperature (day 1)	730	-0.16	**<0.001**	-0.22	**<0.001**	-0.26	**<0.001**	0.06	0.107	-0.19	**<0.001**	-0.35	**<0.001**
Temperature (day 2)	730	-0.16	**<0.001**	-022	**<0.001**	-0.26	**<0.001**	0.06	0.122	-0.20	**<0.001**	-0.35	**<0.001**
Temperature (day 3)	730	-0.16	**<0.001**	-0.23	**<0.001**	-0.26	**<0.001**	0.06	0.119	-0.22	**<0.001**	-0.36	**<0.001**
Pressure (day 0)	730	-0.07	0.079	0.03	0.469	-0.08	**0.038**	0.01	0.773	-0.07	**0.049**	-0.10	**0.007**
Pressure (day 1)	730	0.00	0.931	0.03	0.401	-0.08	**0.028**	0.02	0.696	-0.06	0.134	-0.06	0.127
Pressure (day 2)	730	0.03	0.475	0.01	0.901	-0.07	0.081	0.01	0.845	-0.03	0.374	-0.03	0.440
Pressure (day 3)	730	0.02	0.573	0.01	0.709	-0.01	0.902	0.01	0.731	-0.01	0.792	-0.01	0.812
Humidity (day 0)	730	0.08	**0.036**	0.13	**<0.001**	0.15	**<0.001**	-0.06	0.087	0.09	**0.014**	0.19	**<0.001**
Humidity (day 1)	730	0.09	**0.017**	0.13	**0.001**	0.15	**<0.001**	-0.07	0.066	0.12	**0.001**	0.20	**<0.001**
Humidity (day 2)	730	0.03	0.397	0.15	**<0.001**	0.14	**<0.001**	-0.06	0.140	0.10	**0.006**	0.17	**<0.001**
Humidity (day 3)	730	0.04	0.302	0.12	**0.001**	0.09	**0.011**	-0.02	0.564	0.11	**0.003**	0.15	**<0.001**

COPD = chronic obstructive pulmonary disease; URTI = upper respiratory tract infection; r = Spearman's rank order correlation coefficient; day 0 = day of emergency department (ED) visit; days 1-3 = days before ED visit

ary, and varies in number, size, shape, surface area, and chemical composition[18]. In contact with respiratory epithelium, high concentrations of oxidants and pro-oxidants in environmental pollutants cause the formation of free radicals and initiate inflammatory response through involvement of inflammatory cells and mediators. They reach systemic circulation, leading to subclinical inflammation and negative respiratory and systemic effects. Acute effects are manifested shortly after exposure (hours or days), whereas chronic effects are usually assessed in longitudinal studies over years or decades[18].

Particulate matter particles cause respiratory morbidity and mortality by inducing oxidative stress and inflammation that lead to pulmonary anatomic and physiologic remodeling[19]. Association with PM_{10} has been reported for asthma[20-25], URTI and pneumonia[22], COPD exacerbations[24-28], as well as for all respiratory visits[20,29,30]. In our study, the number of patients with respiratory diseases (except for asthma) correlated with higher PM_{10} concentrations, confirming its role as the most powerful air pollutant generated by burning of fossil fuels in vehicles and other causes.

Nitrogen dioxide is a primary pollutant and strong respiratory irritant, with the main outdoor sources including motor vehicles and fossil-fuel power plants, whereas the most important indoor sources are gas heaters, stoves and tobacco smoke[31,32]. NO_2 is associated with asthma visits[21,23-25,29,33], COPD[22,33,34], URTI[22], pneumonia[29], as well as all respiratory ED visits[35,36]. Samoli *et al*. found significant association of NO_2 with total, cardiovascular and respiratory mortality[31]. Shahi

Table 3. Correlations between air pollutants and occurrence of respiratory diseases (July 2008 – June 2010)

	Days	Pneumonia		Acute bronchitis		COPD		Asthma		URTI		Total	
		r	p	*r*	p	*r*	p	*r*	p	*r*	p	*r*	p
PM_{10} (day 0)	720	0.09	**0.015**	0.12	0.001	0.07	0.063	-0.08	**0.026**	0.08	**0.036**	0.13	**<0.001**
PM_{10} (day 1)	719	0.09	**0.012**	0.07	0.057	0.08	**0.039**	-0.05	0.163	0.09	**0.023**	0.13	**0.001**
PM_{10} (day 2)	718	0.07	0.051	0.09	**0.017**	0.03	0.380	-0.07	**0.049**	0.08	**0.039**	0.10	**0.005**
PM_{10} (day 3)	717	0.06	0.091	0.13	**0.001**	0.04	0.324	-0.06	0.117	0.07	0.075	0.10	**0.007**
NO_2 (day 0)	692	0.10	**0.009**	0.07	0.071	0.06	0.142	0.00	0.963	0.02	0.610	0.11	**0.004**
NO_2 (day 1)	692	0.09	**0.016**	0.03	0.503	0.00	0.933	-0.02	0.621	0.07	0.082	0.07	0.065
NO_2 (day 2)	692	0.03	0.414	0.05	0.176	-0.01	0.759	-0.01	0.899	0.03	0.477	0.04	0.287
NO_2 (day 3)	692	0.05	0.174	0.06	0.115	0.00	0.912	-0.03	0.398	0.06	0.125	0.06	0.110
O_3 (day 0)	646	-0.09	**0.017**	-0.18	**<0.001**	-0.16	**<0.001**	0.08	**0.037**	-0.11	**0.005**	-0.21	**<0.001**
O_3 (day 1)	646	-0.09	**0.021**	-0.15	**<0.001**	-0.15	**<0.001**	0.05	0.191	-0.13	**0.001**	-0.22	**<0.001**
O_3 (day 2)	646	-0.07	0.088	-0.15	**<0.001**	-0.14	**<0.001**	0.06	0.104	-0.15	**<0.001**	-0.21	**<0.001**
O_3 (day 3)	646	-0.07	0.090	-0.15	**<0.001**	-0.14	**<0.001**	0.06	**0.026**	-0.18	**<0.001**	-0.22	**<0.001**

COPD = chronic obstructive pulmonary disease; URTI = upper respiratory tract infection; day 0 = day of emergency department (ED) visit; days 1-3 = days before ED visit; r = Spearman's rank order correlation coefficient

et al. found that altered levels of NO_2 had no effects on respiratory admissions[37]. We found the number of patients with pneumonia to correlate with higher NO_2 concentrations.

Ozone is a powerful oxidant that can damage respiratory tract, causing inflammation and irritation. Several studies report on O_3 to be associated with asthma[22,23,25,34,38], acute and chronic bronchitis[39], URTI[22], and all respiratory visits[27,29,30,38]. Tamayo-Uria *et al*. report that O_3 is negatively associated with COPD[28]. We found the number of patients with asthma to correlate with O_3 concentrations.

Vaduganathan *et al*. investigated the association between exposure to air pollutants (PM_{10} particles) and acute cardiovascular (CV) events[4]. They concluded that increased levels of PM_{10}, even below the current limits set by the European Union, were associated with excess risk of admissions for acute CV events.

The results of our study should be considered in the light of certain limitations. The study period was rather short. The O_3 data were taken from only one monitoring station, which may have led to misclassification of exposure level. Moreover, there is a lack of precise exposure estimates at individual level due to different daily activity patterns and local mobility of each patient. There are many factors that may influence the prevalence of pulmonary disease admissions, which were not taken into account.

In conclusion, weather conditions and air pollutants have a role in the higher occurrence of respiratory diseases in the area with a humid continental climate. We would like to emphasize two important facts, i.e. the need for better cooperation of hydrometeorology services and media on informing the population about weather conditions, and the need to decrease the legally permissible upper limits of air pollution. It is very important because air pollution within the currently permissible levels increases the number of pulmonary patients examined in ED.

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Sažetak

KORELACIJA IZMEĐU POJAVE I POGORŠANJA RESPIRACIJSKIH BOLESTI I ONEČIŠĆENJA ZRAKA UNUTAR DOZVOLJENIH GRANICA

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Željeli smo istražiti nepoznati utjecaj onečišćivača zraka na pojavnost ili pogoršanje bolesti dišnoga sustava u području s vlažnom kontinentalnom klimom. Ova retrospektivna studija je obuhvatila 5868 bolesnika s respiracijskom simptomatologijom (infekcija gornjih dišnih putova (IGDP), upala pluća, akutni bronhitis, kronična opstruktivna plućna bolest (KOPB) i astma) primljenih u hitnu službu. Podaci o broju bolesnika, vrijednostima meteoroloških parametara (srednje dnevne vrijednosti tlaka, temperature zraka i relativne vlage) i koncentracijama čestica onečišćenja zraka (≤10 μm (PM_{10}), ozona (O_3) i dušičnog dioksida (NO_2)) prikupljeni su tijekom dvije godine (srpanj 2008. – lipanj 2010. godine). Bilo je 1839 (31,3%), 1712 (29,2%), 1313 (22,4%), 614 (10,5%) i 390 (6,6%) bolesnika s upalom pluća, KOPB-om, IGDP-om, akutnim bronhitisom i astmom. Srednje dnevne koncentracije NO_2 (25,9 (1,7-89,7) μg/m^3), O_3 (47,1 (4,7-135,4) μg/m^3) i čestica PM_{10} (25,7 (4,6-146,6) μg/m^3) bile su ispod zakonski definirane granične vrijednosti. Među ostalim rezultatima, ukupna pojavnost bolesti dišnoga sustava bila je u pozitivnoj Spearmanovoj korelaciji s vlažnosti zraka (dani 0-3, r=0,15-0,19) i koncentracijom čestica PM_{10} (dani 0-3, r=0,10-0,13) i NO_2 (dan 0, r=0,11), a u negativnoj korelaciji s temperaturom (dani 0-3, r=-0,36 do -0,34) i tlakom zraka (dan 0, r=-0,10) te koncentracijom čestica O_3 (dani 0-3, r=-0,21 do -0,22) (za sve $p<0,05$). U zaključku, pojavnost bolesti dišnoga sustava pokazala je korelaciju s vremenskim uvjetima i onečišćivačima zraka unatoč zakonski dopuštenim vrijednostima u području s vlažnom kontinentalnom klimom.

Ključne riječi: *Onečišćenost zraka – štetno djelovanje; Respiracijski poremećaji; Ozon; Dušikov dioksid; Hrvatska*