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 (PM10), ozone (O3) and nitrogen dioxide (NO2)) were collected dur-
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, re-
spectively. The mean daily concentrations of NO2 (25.9 (1.7-89.7) μg/m3), O3 (47.1 (4.7-135.4) μg/
m3) and PM10 particles (25.7 (4.6-146.6) μg/m3) 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), PM10 (days 0-3, r=0.10 to 0.13) and NO2 concentra-
tions (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 O3 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 diseases1. Climate change increase the amount of pollen and allergen produced by
each plant, mould proliferation, and the concentra-
tions of outdoor ozone (O3) and particulate matter
(PM) at the ground level. The main diseases of concern
are asthma, rhinosinusitis, chronic obstructive pulmo-


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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.

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)\(^1\). 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 \(\chi^2\)-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
with lower values of air temperature (days 0–3), pressure (day 0) and \( \mathrm{O}_3 \) concentration (days 0–3);

b. the occurrence of pneumonia correlated with higher values of air humidity, \( \mathrm{PM}_{10} \) and \( \mathrm{NO}_2 \) concentrations (days 0 and 1), and with lower values of air temperature (days 0–3) and \( \mathrm{O}_3 \) concentration (days 0 and 1);

c. the number of patients with acute bronchitis correlated with higher values of air humidity (days 0–3) and \( \mathrm{PM}_{10} \) concentration (days 2 and 3), and with lower values of air temperature and \( \mathrm{O}_3 \) concentration (days 0–3);

d. the occurrence of COPD correlated with higher values of air humidity (days 0–3) and \( \mathrm{PM}_{10} \) concentration (day 1), and with lower values of air temperature (days 0–3), air pressure (days 0 and 1) and \( \mathrm{O}_3 \) concentration (days 0–3);

e. the occurrence of asthma correlated with higher and lower values of \( \mathrm{O}_3 \) (days 0 and 3) and \( \mathrm{PM}_{10} \) (days 0 and 2) concentrations, respectively; and

f. the occurrence of URTI correlated with higher values of air humidity (days 0–3) and \( \mathrm{PM}_{10} \) concentration (days 0–2), and with lower values of air temperature (days 0–3), air pressure (day 0) and \( \mathrm{O}_3 \) 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\(^9\)–\(^\text{11}\), 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Male (median and range)</th>
<th>Female (median and range)</th>
<th>Mann-Whitney U test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>69 (17-97)</td>
<td>74 (16-99)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>52 (15-91)</td>
<td>60 (18-96)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>74 (20-93)</td>
<td>76 (17-100)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Asthma</td>
<td>36 (15-88)</td>
<td>49 (15-86)</td>
<td>p=0.005</td>
</tr>
<tr>
<td>URTI</td>
<td>43 (14-92)</td>
<td>42 (13-98)</td>
<td>p=0.265</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Days</th>
<th>Pneumonia</th>
<th>Acute bronchitis</th>
<th>COPD</th>
<th>Asthma</th>
<th>URTI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
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<td></td>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>Temperature (day 0)</td>
<td>-0.15</td>
<td>&lt;0.001</td>
<td>-0.23</td>
<td>&lt;0.001</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temperature (day 1)</td>
<td>-0.16</td>
<td>&lt;0.001</td>
<td>-0.22</td>
<td>&lt;0.001</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temperature (day 2)</td>
<td>-0.16</td>
<td>&lt;0.001</td>
<td>-0.22</td>
<td>&lt;0.001</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temperature (day 3)</td>
<td>-0.16</td>
<td>&lt;0.001</td>
<td>-0.23</td>
<td>&lt;0.001</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pressure (day 0)</td>
<td>-0.07</td>
<td>0.079</td>
<td>0.03</td>
<td>0.469</td>
<td>-0.08</td>
<td>0.038</td>
</tr>
<tr>
<td>Pressure (day 1)</td>
<td>0.00</td>
<td>0.931</td>
<td>0.03</td>
<td>0.401</td>
<td>-0.08</td>
<td>0.028</td>
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<tr>
<td>Pressure (day 2)</td>
<td>0.03</td>
<td>0.475</td>
<td>0.01</td>
<td>0.901</td>
<td>-0.07</td>
<td>0.081</td>
</tr>
<tr>
<td>Pressure (day 3)</td>
<td>0.02</td>
<td>0.573</td>
<td>0.01</td>
<td>0.709</td>
<td>-0.01</td>
<td>0.902</td>
</tr>
<tr>
<td>Humidity (day 0)</td>
<td>0.08</td>
<td>0.036</td>
<td>0.13</td>
<td>&lt;0.001</td>
<td>0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Humidity (day 1)</td>
<td>0.09</td>
<td>0.017</td>
<td>0.13</td>
<td>0.001</td>
<td>0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Humidity (day 2)</td>
<td>0.03</td>
<td>0.397</td>
<td>0.15</td>
<td>&lt;0.001</td>
<td>0.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Humidity (day 3)</td>
<td>0.04</td>
<td>0.302</td>
<td>0.12</td>
<td>0.001</td>
<td>0.09</td>
<td>0.011</td>
</tr>
</tbody>
</table>

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\textsuperscript{19}. 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 sub-clinical 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\textsuperscript{18}.

Particulate matter particles cause respiratory morbidity and mortality by inducing oxidative stress and inflammation that lead to pulmonary anatomic and physiologic remodeling\textsuperscript{19}. Association with PM\textsubscript{10} has been reported for asthma\textsuperscript{20-25}, URTI and pneumonia\textsuperscript{22}, COPD exacerbations\textsuperscript{24-28}, as well as for all respiratory visits\textsuperscript{20,29,30}. In our study, the number of patients with respiratory diseases (except for asthma) correlated with higher PM\textsubscript{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\textsuperscript{31,32}. NO\textsubscript{2} is associated with asthma visits\textsuperscript{21,23-25,29,33}, COPD\textsuperscript{22,33,34}, URTI\textsuperscript{22}, pneumonia\textsuperscript{29}, as well as all respiratory ED visits\textsuperscript{35,36}. Samoli \textit{et al.} found significant association of NO\textsubscript{2} with total, cardiovascular and respiratory mortality\textsuperscript{31}.

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

<table>
<thead>
<tr>
<th></th>
<th>Days</th>
<th>Pneumonia</th>
<th>Acute bronchitis</th>
<th>COPD</th>
<th>Asthma</th>
<th>URTI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>PM\textsubscript{10}</td>
<td>day 0</td>
<td>720</td>
<td>0.09</td>
<td>0.015</td>
<td>0.12</td>
<td>0.001</td>
<td>0.07</td>
</tr>
<tr>
<td>PM\textsubscript{10}</td>
<td>day 1</td>
<td>719</td>
<td>0.09</td>
<td>0.012</td>
<td>0.07</td>
<td>0.057</td>
<td>0.08</td>
</tr>
<tr>
<td>PM\textsubscript{10}</td>
<td>day 2</td>
<td>718</td>
<td>0.07</td>
<td>0.051</td>
<td>0.09</td>
<td>0.017</td>
<td>0.03</td>
</tr>
<tr>
<td>PM\textsubscript{10}</td>
<td>day 3</td>
<td>717</td>
<td>0.06</td>
<td>0.091</td>
<td>0.13</td>
<td>0.001</td>
<td>0.04</td>
</tr>
<tr>
<td>NO\textsubscript{2}</td>
<td>day 0</td>
<td>692</td>
<td>0.10</td>
<td>0.009</td>
<td>0.07</td>
<td>0.071</td>
<td>0.06</td>
</tr>
<tr>
<td>NO\textsubscript{2}</td>
<td>day 1</td>
<td>692</td>
<td>0.09</td>
<td>0.016</td>
<td>0.03</td>
<td>0.503</td>
<td>0.00</td>
</tr>
<tr>
<td>NO\textsubscript{2}</td>
<td>day 2</td>
<td>692</td>
<td>0.03</td>
<td>0.414</td>
<td>0.05</td>
<td>0.176</td>
<td>-0.01</td>
</tr>
<tr>
<td>NO\textsubscript{2}</td>
<td>day 3</td>
<td>692</td>
<td>0.05</td>
<td>0.174</td>
<td>0.06</td>
<td>0.115</td>
<td>0.00</td>
</tr>
<tr>
<td>O\textsubscript{3}</td>
<td>day 0</td>
<td>646</td>
<td>-0.09</td>
<td>0.017</td>
<td>-0.18</td>
<td>&lt;0.001</td>
<td>-0.16</td>
</tr>
<tr>
<td>O\textsubscript{3}</td>
<td>day 1</td>
<td>646</td>
<td>-0.09</td>
<td>0.021</td>
<td>-0.15</td>
<td>&lt;0.001</td>
<td>-0.15</td>
</tr>
<tr>
<td>O\textsubscript{3}</td>
<td>day 2</td>
<td>646</td>
<td>-0.07</td>
<td>0.088</td>
<td>-0.15</td>
<td>&lt;0.001</td>
<td>-0.14</td>
</tr>
<tr>
<td>O\textsubscript{3}</td>
<td>day 3</td>
<td>646</td>
<td>-0.07</td>
<td>0.090</td>
<td>-0.15</td>
<td>&lt;0.001</td>
<td>-0.14</td>
</tr>
</tbody>
</table>

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 NO₃ had no effects on respiratory admissions. We found the number of patients with pneumonia to correlate with higher NO₂ concentrations.

Ozone is a powerful oxidant that can damage respiratory tract, causing inflammation and irritation. Several studies report on O₃ to be associated with asthma, acute and chronic bronchitis, URTI, and all respiratory visits. Tamayo-Uria et al. report that O₃ is negatively associated with COPD. We found the number of patients with asthma to correlate with O₃ concentrations.

Vaduganathan et al. investigated the association between exposure to air pollutants (PM₁₀ particles) and acute cardiovascular (CV) events. They concluded that increased levels of PM₁₀ 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 O₃ 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.

References


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 vremenškim 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