Number of total mortality, cardiovascular mortality and Chronic Obstructive Pulmonary Disease due to exposure with Nitrogen dioxide in Tehran during 2005-2014

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Abstract
Background & Aims: Air pollution has adverse effects on human health and cause various diseases including cardiovascular disease and respiratory. Therefore this study with aim of study of Number of total mortality, cardiovascular mortality and Chronic Obstructive Pulmonary Disease due to exposure with Nitrogen dioxide in Tehran during 2005-2014 were performed.

Materials & Methods: This study is a descriptive-analytic. At first hourly data were taken from Tehran environmental protection agency and Air Quality Control Company. Then validated according to the WHO guidelines and Statistical parameters for quantifying health effects were calculated in excel. Finally, assessment of cases total mortality with software was performed.

Results: The results showed that the number of total mortality caused by exposure to NO2 In the past decade is 15141 people. Also the total number of cardiovascular mortality in the past decade is 8480 people and the total number of Chronic Obstructive Pulmonary Disease in the past decade is 2454 people in 2005-2014 years.

Conclusion: Air pollution, especially nitrogen dioxide leads to mortality And Morbidity in a lot of people. According to the results of this study should such actions, policies and planning and management to reduce air pollution preparedness of hospitals and health centers, educating the public

Keywords: Air pollution, total mortality, Chronic Obstructive Pulmonary Disease, Nitrogen dioxide

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Introduction
Air pollution, caused by modern life, is considered as one of the great problems of large cities such as Tehran. It can be understood according to multiple studies that the phenomenon has significant environmental and health effects on human and the environment (1-5). Air pollution is known as a major reason for increased mortality in the world. So that the mortalities have reached from 800 thousand cases in 2000 to 7.3 million in 2012. In the meantime, 65 percent of these mortalities relates to the continent of Asia.

Seeping into sensitive areas or deep in the lungs, air pollutants are causing respiratory diseases such as emphysema and bronchitis. They can also lead to the aggravation of cardiovascular diseases, increase utilization and hospital admissions and premature death.
According to World Health Organization report, in 2012, approximately 3.7 million people worldwide lose their lives due to air pollution (9). Nowadays, many major cities have faced the difficult situation of unfavorable air quality and air quality status is not suitable in many metropolitan cities, especially Tehran (10-17). Gaseous pollutants such as nitrogen dioxide (NO₂), sulfur dioxide (SO₂), ozone (O₃) and Carbon monoxide (CO) also exert adverse effects on mortality which necessitates their reviewing (18-20). Nitrogen (NOₓ) and mainly nitric oxide (NO) are produced by high-temperature combustion processes such as the burning of fuels in motors of vehicles and power plants, which once the dispersion occurs, NO reacts relatively fast with oxygen or ozone and forms NO₂. These reactions are dominant and known as secondary source of NO₂ production and the deformation often occurs near the source of contamination.

It should be noted that the air inside as well as outside can be contaminated with high concentrations of NO₂ because no air heaters and ovens emit significant amounts of pollutants (21). Reddish-orange NO₂ (almost brown) has a boiling point of 21.2 degrees Celsius and the pressure is low which holds it in its gaseous state. The gas is a strong oxidant and corrosive and is lower respiratory tract simulator, physiologically. According to the results of studies, toxicity of NO₂ is several times more than NO causing effects on humans such as changes in the tissues of the kidney, liver and heart after 2 hours at a concentration of 15 ppm. It reduces immunity against infectious diseases, susceptibility to bacterial and increased risk of viral infections (22).

The main mechanism of toxicity of NO₂ has been attributed to intervene lipid peroxidation in the cell membrane and different effects of free radical on structural and functional molecules (21). According to the results of the studies, the main impact of NO₂ on people who were exposed to these contaminants was respiratory allergy, usually occurs in concentrations more than 1,800 micrograms per cubic meter in healthy subjects and in concentrations of 200 to 500 micrograms per cubic meter in people with asthma (23) or chronic obstructive pulmonary disease (COPD) (24). There are different models to evaluate the effects of air pollutants on human health, most of which are Epidemiological-Statistical and integrated air quality data at concentration intervals with epidemiological parameters such as relative risk, baseline incidence and the relative component and display the result in mortality. One of these models is AirQ 2.2.3 software where the information of connection-response of population exposure data has been combined and the expected health effects are estimated. AirQ is a specialized software that enables the user to assess the potential effects of specific pollutants on human in an urban area and specific time period. AirQ is composed of two distinct parts. The first part contains the number of cases and mortalities attributable to air pollution (based on risk estimates from Time Series studies) and the second is to estimate long-term exposure effects using life tables (based on the estimation of the risks from Cohort Studies) (25).

Tehran is among Iran's great metropolises where the level of air pollution has increased day after day and became more severe. It must be noted that the dense of pollution at the level of citizens respiratory is an alarm that increases cardiovascular diseases, pulmonary, cancer and warns the mortality. Given the current trends, the mortalities are expected to be increased in Tehran yearly and more attentions of officials and experts is necessary to control air pollution. One of the most important ways to control the air pollution in large cities is management programs in which the correct formulation of the program would not be possible without relying on sources of accurate information on the status of ambient air and its impact on human health. Given that the health effects by air pollution with the contaminations have not been investigated...
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scientifically, this study analyzes the effects of NO\textsubscript{2} on the health of the citizens of Metropolis Tehran over a ten-year process using a model and AirQ software.

**Materials and Methods**

This is a cross-sectional study and AirQ 2.2.3 software was used to assess the adverse effects of NO\textsubscript{2} on the health of citizens in Tehran. The information of NO\textsubscript{2} emissions was received both from environmental protection agencies and Tehran Air Quality Control Company in Microsoft Excel file format as hourly data.

The data validity should be examined in order to perform statistical analysis and using raw data, in which the criteria listed by World Health Organization (WHO) was used for the purpose. Some of these criteria include: the ratio between the numbers of valid data for the two seasons (warm and cold) should not be more than 2, at least 75% of valid data must exist in order to achieve the average one-hour values from data with a shorter average time, at least 75% of one-hour data (18 hours) should exist and be valid to access the values of the eight-hour moving average form one-hour data, and etc. (25). Valid data, after discarding the invalid data, must be entered into the software, but it should be considered that the data are based on volume-volume (ppm) and since determining adverse health effects are associated with inhaled pollutants’ mass in AirQ, the data were converted using Microsoft Excel with regard to temperature and pressure conditions and were written based on volume-weight (μg/m\textsuperscript{3}).

Pre-processing steps (including removal, sheeting pollutant and time integration to estimate the average) and secondary processing (including code writing, calculating the mean and modifying the condition) have been done after the conversion using Microsoft Excel, and finally the required statistics including annual mean, heating season average, cold season average, 98\textsuperscript{th} percentile, annual maximum, warm season maximum and cold season maximum have been measured, respectively in each of the studied years. Population information was taken from the Statistical Center of Iran to determine each year population, which is required to estimate the health effects of pollutants. Finally, related component, the number of mortalities and mortalities from cardiovascular and respiratory diseases caused by exposure to O3 pollutant are presented in both form of tables and graphs by entering the data processed results in Air Q. To calculate the health effects and consequences in the Air Q, two ways can be used:

1. The use of WHO default values for the grade incidence and relative risk (95% confidence intervals). The values are automatically displayed to run the program.

2. Replacement of the default values with the self-estimates of grade and relative risk (95% confidence intervals) using regional and national epidemiological studies.

Because of diverse differences between Iran and Europe in the age pyramid, default data of the software cannot be used as for the European Community. For this purpose, relative risks calculated for the country have been used through literature review (26, 27)

<table>
<thead>
<tr>
<th>Health effects</th>
<th>Incidence</th>
<th>RR (95% CI) per 10μg.m\textsuperscript{3} NO\textsubscript{2}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Overall mortality</td>
<td>5.543</td>
</tr>
<tr>
<td></td>
<td>Mortalities from cardiovascular disease</td>
<td>231</td>
</tr>
<tr>
<td>Disease</td>
<td>Hospitalization due to chronic obstructive pulmonary</td>
<td>4.101</td>
</tr>
</tbody>
</table>

* The numbers in parentheses represent the low and high limits of relative risk.
Results

The results of this study include statistical parameters about concentration of nitrogen dioxide in Tehran during 2005-2014 and the results obtained from the application tables and charts are provided in this section. After validation of the data received from Air Quality Control and the Department of Environment in accordance with the standards of WHO, the number of stations with valid data for the analysis of nitrogen dioxide in Tehran during 2005-2010 were respectively as 5, 6, 6, 5, 8, 15, 11, 25, 9 and 21 stations selected from 11 stations in 2005, 14 stations in 2006, 14 stations in 2007, 15 stations in 2008, 18 stations in 2009, 37 stations in 2010, 36 stations in 2011, 42 stations in 2012, 35 stations in 2013 and 33 stations in 2014, respectively. After primary and secondary processing of raw data, the required measures for the model are calculated, determined and presented in Table 2.

Table 2: Indicators necessary to assess the effects of NO$_2$ and the ratio of average annual concentration (µg / m$^3$) to standards during 2005-2014

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual average</td>
<td>95</td>
<td>108</td>
<td>166</td>
<td>205</td>
<td>126</td>
<td>131</td>
<td>92</td>
<td>86</td>
<td>101</td>
<td>96</td>
</tr>
<tr>
<td>Cold season average</td>
<td>100</td>
<td>108</td>
<td>201</td>
<td>237</td>
<td>133</td>
<td>145</td>
<td>96</td>
<td>85</td>
<td>110</td>
<td>104</td>
</tr>
<tr>
<td>Warm season average</td>
<td>90</td>
<td>109</td>
<td>132</td>
<td>174</td>
<td>119</td>
<td>117</td>
<td>89</td>
<td>86</td>
<td>92</td>
<td>88</td>
</tr>
<tr>
<td>Annual 98th percentile</td>
<td>106</td>
<td>147</td>
<td>177</td>
<td>250</td>
<td>185</td>
<td>188</td>
<td>119</td>
<td>118</td>
<td>116</td>
<td>143</td>
</tr>
<tr>
<td>Annual maximum</td>
<td>261</td>
<td>356</td>
<td>386</td>
<td>644</td>
<td>297</td>
<td>228</td>
<td>218</td>
<td>122</td>
<td>173</td>
<td>174</td>
</tr>
<tr>
<td>Cold season maximum</td>
<td>261</td>
<td>356</td>
<td>386</td>
<td>644</td>
<td>297</td>
<td>228</td>
<td>173</td>
<td>122</td>
<td>197</td>
<td>174</td>
</tr>
<tr>
<td>Warm season maximum</td>
<td>173</td>
<td>178</td>
<td>213</td>
<td>334</td>
<td>183</td>
<td>208</td>
<td>218</td>
<td>121</td>
<td>137</td>
<td>128</td>
</tr>
</tbody>
</table>

The ratio of average annual concentration (µg / m$^3$) to standards

| Standard=A=40µg/m$^3$ | 2.37 | 2.72 | 4.15 | 5.13 | 3.15 | 3.28 | 2.32 | 2.15 | 2.52 | 2.4  |
| Standard=B=100µg/m$^3$ | 0.95 | 1.08 | 1.66 | 2.05 | 1.26 | 1.31 | 0.92 | 0.86 | 1.01 | 0.96 |

B: EPA’s AirQuality National standards

Based on the results of AirQ, the number of additional items and related component to NO$_2$ for overall mortalities, mortalities due to cardiovascular disease and hospitalizations due to chronic obstructive pulmonary disorder (COPD) have been estimated and are shown in Table 3.
Table 3: Estimated values for the number of additional items and related component to NO2 for overall mortalities, mortalities due to cardiovascular disease and hospitalizations due to chronic obstructive pulmonary disorder during mentioned years

<table>
<thead>
<tr>
<th>Health consequences</th>
<th>Attributable (Related component)</th>
<th>85</th>
<th>86</th>
<th>87</th>
<th>88</th>
<th>89</th>
<th>90</th>
<th>91</th>
<th>92</th>
<th>93</th>
</tr>
</thead>
<tbody>
<tr>
<td>The number of additional items and related component to NO2 for overall mortalities</td>
<td>Upper limit</td>
<td>3.3</td>
<td>3.83</td>
<td>6.06</td>
<td>6.91</td>
<td>4.43</td>
<td>4.67</td>
<td>3.2</td>
<td>2.95</td>
<td>3.52</td>
</tr>
<tr>
<td></td>
<td>Middle limit</td>
<td>2.5</td>
<td>2.9</td>
<td>4.61</td>
<td>5.27</td>
<td>3.36</td>
<td>3.54</td>
<td>2.42</td>
<td>2.23</td>
<td>2.66</td>
</tr>
<tr>
<td></td>
<td>Lower limit</td>
<td>1.68</td>
<td>1.95</td>
<td>3.12</td>
<td>3.58</td>
<td>2.26</td>
<td>2.39</td>
<td>1.62</td>
<td>1.5</td>
<td>1.79</td>
</tr>
<tr>
<td>Related component (%)</td>
<td>Upper limit</td>
<td>1456</td>
<td>1730</td>
<td>2778</td>
<td>3215</td>
<td>2092</td>
<td>2235</td>
<td>1555</td>
<td>1455</td>
<td>1758</td>
</tr>
<tr>
<td></td>
<td>Middle limit</td>
<td>1101</td>
<td>1310</td>
<td>2116</td>
<td>2453</td>
<td>1586</td>
<td>1714</td>
<td>1100</td>
<td>1330</td>
<td>1274</td>
</tr>
<tr>
<td></td>
<td>Lower limit</td>
<td>740</td>
<td>882</td>
<td>1432</td>
<td>1665</td>
<td>1144</td>
<td>790</td>
<td>738</td>
<td>894</td>
<td>856</td>
</tr>
<tr>
<td>The number of additional items and related component to NO2 for mortalities due to cardiovascular disease</td>
<td>Extra cases</td>
<td>Upper limit</td>
<td>4.10</td>
<td>4.74</td>
<td>7.46</td>
<td>8.49</td>
<td>5.48</td>
<td>5.77</td>
<td>3.97</td>
<td>3.67</td>
</tr>
<tr>
<td></td>
<td>Middle limit</td>
<td>3.3</td>
<td>3.83</td>
<td>6.06</td>
<td>6.91</td>
<td>4.43</td>
<td>4.67</td>
<td>3.2</td>
<td>2.95</td>
<td>3.52</td>
</tr>
<tr>
<td></td>
<td>Lower limit</td>
<td>2.5</td>
<td>2.9</td>
<td>4.61</td>
<td>5.27</td>
<td>3.36</td>
<td>3.54</td>
<td>2.42</td>
<td>2.23</td>
<td>2.66</td>
</tr>
<tr>
<td></td>
<td>Related</td>
<td>Upper limit</td>
<td>767</td>
<td>910</td>
<td>1454</td>
<td>1679</td>
<td>1099</td>
<td>1174</td>
<td>819</td>
<td>767</td>
</tr>
<tr>
<td></td>
<td>Middle limit</td>
<td>618</td>
<td>735</td>
<td>1180</td>
<td>1366</td>
<td>889</td>
<td>950</td>
<td>661</td>
<td>747</td>
<td>716</td>
</tr>
<tr>
<td></td>
<td>Lower limit</td>
<td>468</td>
<td>556</td>
<td>899</td>
<td>1042</td>
<td>674</td>
<td>721</td>
<td>449</td>
<td>467</td>
<td>565</td>
</tr>
<tr>
<td>The number of additional items and related component to NO2 for hospitalizations due to chronic obstructive pulmonary disorder</td>
<td>The number of additional</td>
<td>Upper limit</td>
<td>3.62</td>
<td>4.19</td>
<td>6.62</td>
<td>7.55</td>
<td>4.85</td>
<td>5.11</td>
<td>3.51</td>
<td>3.24</td>
</tr>
<tr>
<td></td>
<td>cases (cases)</td>
<td>2.17</td>
<td>2.52</td>
<td>4.02</td>
<td>4.6</td>
<td>2.92</td>
<td>3.08</td>
<td>2.10</td>
<td>1.94</td>
<td>2.31</td>
</tr>
<tr>
<td></td>
<td>Related</td>
<td>Upper limit</td>
<td>297</td>
<td>353</td>
<td>566</td>
<td>655</td>
<td>427</td>
<td>456</td>
<td>318</td>
<td>297</td>
</tr>
<tr>
<td></td>
<td>component (%)</td>
<td>Middle limit</td>
<td>178</td>
<td>212</td>
<td>344</td>
<td>399</td>
<td>257</td>
<td>275</td>
<td>190</td>
<td>178</td>
</tr>
<tr>
<td></td>
<td>Lower limit</td>
<td>41</td>
<td>50</td>
<td>82</td>
<td>95</td>
<td>60</td>
<td>65</td>
<td>44</td>
<td>41</td>
<td>50</td>
</tr>
</tbody>
</table>

AirQ model is plotting a graph for the concentration intervals of pollutants for individual health effects which demonstrates the health effect of pollutants in contact with various concentrations of pollutants. Due to the high number of charts, graphs of the early years and end years of the study (Figures 1 to 6) are satisfied. As shown in Figures 1 to 6, there are three curves in each graph that the curves were drawn based on relative risks (upper, middle and lower limits) shown in Table 1.

Graph 1: Cumulative cases of death from the NO2 against concentration intervals in 2005
Graph 2. Cumulative number of cardiovascular mortalities caused by NO$_2$ against concentration intervals in 2005.

Graph 3. Cumulative number of hospitalization due to chronic obstructive pulmonary caused by NO$_2$ against concentration intervals in 2005.
Number of total mortality, cardiovascular mortality and Chronic Obstructive Pulmonary Disease mortality caused by NO2 against concentration intervals in 2014

Graph 4. Cumulative number of overall mortalities caused by NO2 against concentration intervals in 2014

Graph 5. Cumulative number of cardiovascular mortalities caused by NO2 against concentration intervals in 2014

Graph 6. Cumulative number of hospitalization due to chronic obstructive pulmonary caused by NO2 against concentration intervals in 2014
Conclusion

It can be seen, according to Table 2, that the average concentration of NO$_2$ in cold season was more than warm season over the studied ten years which is linked to high consumption of fuel by cars, use of gas by homes for heating and etc. and also, non-destruction of produced NO$_2$ due to lack of sunlight in winter. Compared to the annual average concentrations of guidelines and standard values (Table 2), it is determined that the annual average of NO$_2$ concentration was above the standard level over the research years and the need for further studies about its effects on health is identified. In a study on five megacities in Iran during 2011, Bahrami et al. showed that the average annual concentration of NO$_2$ in the cold season in all the examined cities was more than warm season. Furthermore, average annual concentrations were above the standard level in all cities and has been the guiding values (1). In considering the total number of mortalities, 2007 and 2008 have the most relative component and the highest number of cumulative total death with grade incidence equal to 543.5 cases per hundred thousand and the relative risk of 1.003. Death by cardiovascular disease with baseline incidence of 231 cases per hundred thousand people and the relative risk of 1.004 and hospitalization due to chronic obstructive pulmonary with baseline incidence of 101.4 people per hundred thousand people and the relative risk of 1.0026 had the highest relative component in 2008 and the highest cumulative number of cardiovascular death and referring to hospital emergency due to chronic obstructive pulmonary disease were as 1366 and 399 people, respectively. In a study by Ghanbari et al. in 2014 entitled "The effect of exposure to NO$_2$, O$_3$, SO$_2$ on hospitalization due to chronic obstructive pulmonary in Tabriz ", showed that there is a direct correlation between exposure to gas pollutants and respiratory diseases and chronic obstructive pulmonary, so that 32, 69 and 15 hospitalization cases have been observed due to chronic obstructive pulmonary disease during a year in Tabriz (28). This can be due to the high number of vehicles, increased traffic and subsequently non-standard fuel highly consumption in vehicles, high permanent and temporary population in Tehran. During the study by Burnett et al. conducted for 14 years in Toronto, Canada, the average annual number of hospital admissions due to chronic obstructive pulmonary disease were about 8 people that 40.4% has been reported because of exposure to NO$_2$ (29).

Goudarzi and his colleagues used AirQ model to assess the health effects of NO$_2$ in Tehran in 2008 and reported that the concentrations of NO$_2$ over 60 micrograms per cubic meter relate to 3.4 percent of all mortalities, cardiovascular and heart diseases and hospital admissions due to chronic lung disease (30). Touloumi and colleagues also reported a significant relationship between NO$_2$ and the daily mortalities (31). The results indicate the adverse effects of NO$_2$ on health. A single pollutant can act as an indicator of a pollutant mixtures. NO$_2$ can be considered as an indicator of other produced pollutants such as particulate matter from the exhaust of vehicles. Population growth causing excessive development of factories without environmental considerations, and increased use of fossil fuels are the main reasons of air pollution increment. Generally, the statistics related to the number of mortalities, cardiovascular disease and chronic obstructive pulmonary clearly indicate the effects of air pollution on the health of citizens; hence there is a need for proper and effective planning to control and reduce the harmful effects of air pollutants, especially NO$_2$.

Quantification of the effects attributed to air pollution determines the impact of air pollutants on population, and clearly shows the critical situation of air quality. Obtaining a direct relationship between exposing to different concentrations of the pollutants
and their effects on human health is very difficult. The method is one of the validated methods used to assess health effects attributed to air pollution. The results of this study and software output show that the cumulative number of mortalities, mortalities by cardiovascular disease, and hospitalization due to chronic obstructive pulmonary disease caused by air pollution involves a lot in Tehran and the decision-makers and authorities should operate functional, sustainable and feasible solutions and strategies to reduce and control air pollution in Tehran metropolis based on studies and scientific research.

Acknowledgments

Present article is part of a research project entitled “Assessment of health effects of air pollution on the number of mortalities, cardiovascular and respiratory diseases in Tehran metropolis and analysis of air quality indicators during 2005-2014 ”, adopted by University of Medical Sciences and health services in Iran in 2014, code number 25455, which has been implemented by University of Medical Sciences. The authors deem themselves necessary to thank and appreciate the cooperation of respected authorities of Tehran quality control Company and Tehran environmental Protection Bureau for data collection.

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