

# 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 NO<sub>2</sub> 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

Be done.

**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

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(6-8). 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 ( $\text{NO}_2$ ), sulfur dioxide ( $\text{SO}_2$ ), ozone ( $\text{O}_3$ ) and Carbon monoxide (CO) also exert adverse effects on mortality which necessitates their reviewing (18-20). Nitrogen ( $\text{NO}_x$ ) 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  $\text{NO}_2$ . These reactions are dominant and known as secondary source of  $\text{NO}_2$  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  $\text{NO}_2$  because no air heaters and ovens emit significant amounts of pollutants (21). Reddish-orange  $\text{NO}_2$  (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  $\text{NO}_2$  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  $\text{NO}_2$  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  $\text{NO}_2$  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

scientifically, this study analyzes the effects of NO<sub>2</sub> 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<sub>2</sub> on the health of citizens in Tehran. The information of NO<sub>2</sub> 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 from 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 ( $\mu\text{g}/\text{m}^3$ ). 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<sup>th</sup> 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 O<sub>3</sub> 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 1:** values for relative risk and incidence of the use of models to suit different health effects of nitrogen dioxide (26, 27)

	(Health effects)	Incidence	RR (95% CI) per 10 $\mu\text{g}/\text{m}^3$ NO <sub>2</sub>
Death	Overall mortality	5.543	003.1(002.1– 004.1)
	Mortalities from cardiovascular disease	231	004.1(003.1– 005.1)
Disease	Hospitalization due to chronic obstructive pulmonary	4.101	0026.1(0006.1– 0044.1)

\* 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<sub>2</sub> and the ratio of average annual concentration (µg / m<sup>3</sup>) to standards during 2005-2014

Parameter	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Annual average	95	108	166	205	126	131	92	86	101	96
Cold season average	100	108	201	237	133	145	96	85	110	104
Warm season average	90	109	132	174	119	117	89	86	92	88
Annual 98th percentile	196	174	322	450	183	208	139	119	156	143
Annual maximum	261	356	386	644	297	228	218	122	197	174
Cold season maximum	261	356	386	644	297	228	173	122	197	174
Warm season maximum	173	178	213	334	183	208	218	121	137	128
The ratio of average annual concentration (µg / m <sup>3</sup> ) to standards										
StandardA=40µg/m <sup>3</sup>	2.37	2.72	4.15	5.13	3.15	3.28	2.32	2.15	2.52	2.4
StandardB=100µg/m <sup>3</sup>	0.95	1.08	1.66	2.05	1.26	1.31	0.92	0.86	1.01	0.96

A: Iran national standard (ratified in 2009), Guidelines for WHO (2005), Europe Union standard (2012)

B: EPA's AirQuality National standards

Based on the results of AirQ, the number of additional items and related component to NO<sub>2</sub> for overall mortalities, mortalities due to cardiovascular

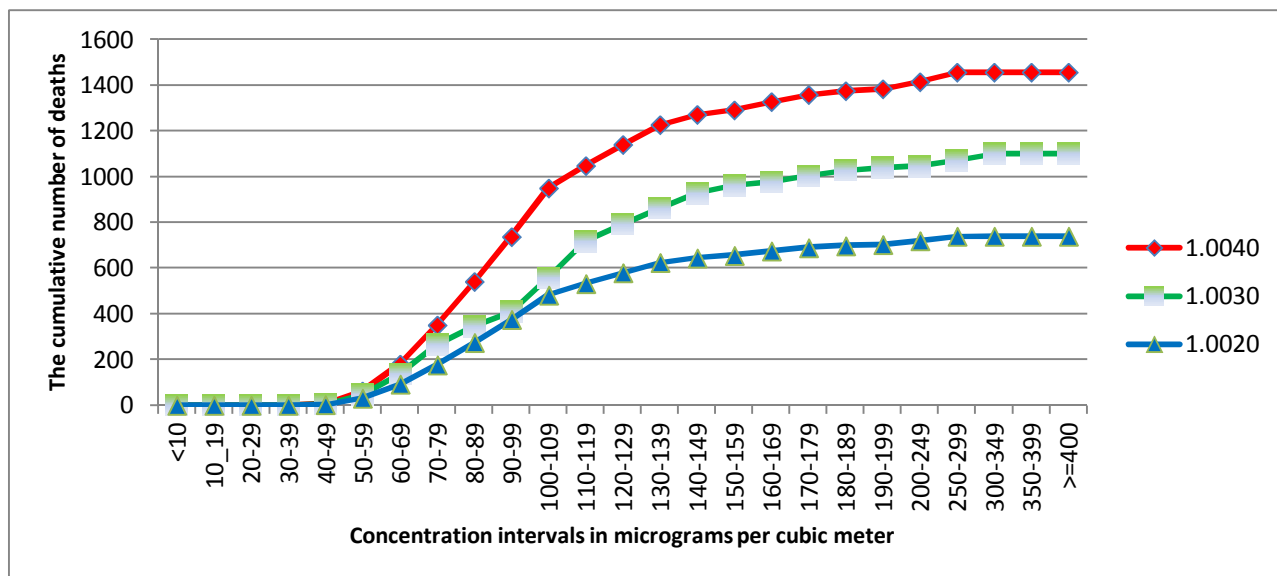
disease and hospitalizations due to chronic obstructive pulmonary disorder (COPD) have been estimated and are shown in Table 3.

**Table 3:** Estimated values for the number of additional items and related component to NO<sub>2</sub> for overall mortalities, mortalities due to cardiovascular disease and hospitalizations due to chronic obstructive pulmonary disorder during mentioned years

Health consequences			85	86	87	88	89	90	91	92	93	
The number of additional items and related component to NO <sub>2</sub> for overall mortalities	Attributable component (%)	Upper limit	3.3	3.83	6.06	6.91	4.43	4.67	3.2	2.95	3.52	3.32
		Middle limit	2.5	2.9	4.61	5.27	3.36	3.54	2.42	2.23	2.66	2.51
		Lower limit	1.68	1.95	3.12	3.58	2.26	2.39	1.62	1.5	1.79	1.69
Related component (%)	Extra cases	Upper limit	1456	1730	2778	3215	2092	2235	1555	1455	1758	1684
		Middle limit	1101	1310	2116	2453	1586	1696	1175	1100	1330	1274
		Lower limit	740	882	1432	1665	1069	1144	790	738	894	856
The number of additional items and related component to NO <sub>2</sub> for mortalities due to cardiovascular disease	Related component (%)	Upper limit	4.10	4.74	7.46	8.49	5.48	5.77	3.97	3.67	4.36	4.12
		Middle limit	3.3	3.83	6.06	6.91	4.43	4.67	3.2	2.95	3.52	3.32
		Lower limit	2.5	3.9	4.61	5.27	3.36	3.54	2.42	2.23	2.66	2.51
The number of additional items and related component to NO <sub>2</sub> for hospitalizations due to chronic obstructive pulmonary disorder	The number of additional cases (cases)	Upper limit	767	910	1454	1679	1099	1174	819	767	926	887
		Middle limit	618	735	1180	1366	889	950	661	618	747	716
		Lower limit	468	556	899	1042	674	721	449	467	565	541
The number of additional items and related component to NO <sub>2</sub> for hospitalizations due to chronic obstructive pulmonary disorder	Related component (%)	Upper limit	3.62	4.19	6.62	7.55	4.85	5.11	3.51	3.24	3.85	3.64
		Middle limit	2.17	2.52	4.02	4.6	2.92	3.08	2.10	1.94	2.31	2.18
		Lower limit	0.51	0.59	0.95	1.10	0.69	0.73	0.49	0.45	0.54	0.51
The number of additional items and related component to NO <sub>2</sub> for hospitalizations due to chronic obstructive pulmonary disorder	Related component (%)	Upper limit	297	353	566	655	427	456	318	297	359	344
		Middle limit	178	212	344	399	257	275	190	178	215	206
		Lower limit	41	50	82	95	60	65	44	41	50	48

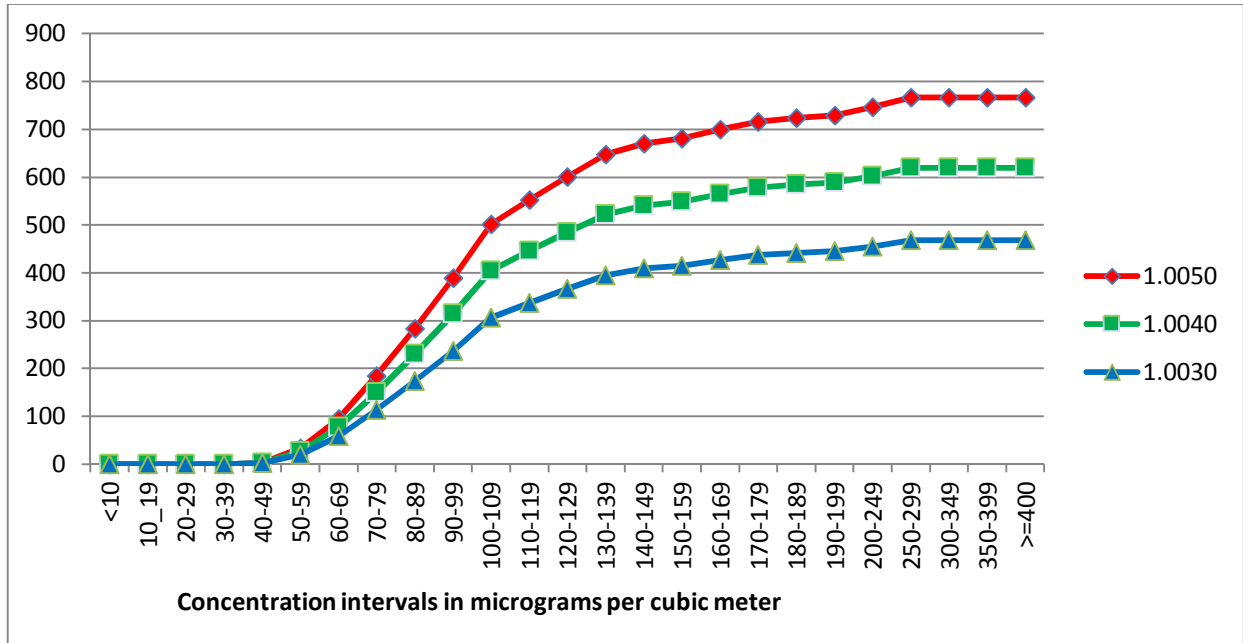
AirQ model is plotting a graph for the concentration intervals of pollutants for individual health effects which demonstrates the health effect of pollutants in contact with various concentrations of pollutants. Due to the high number of charts, graphs of the early years and

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.

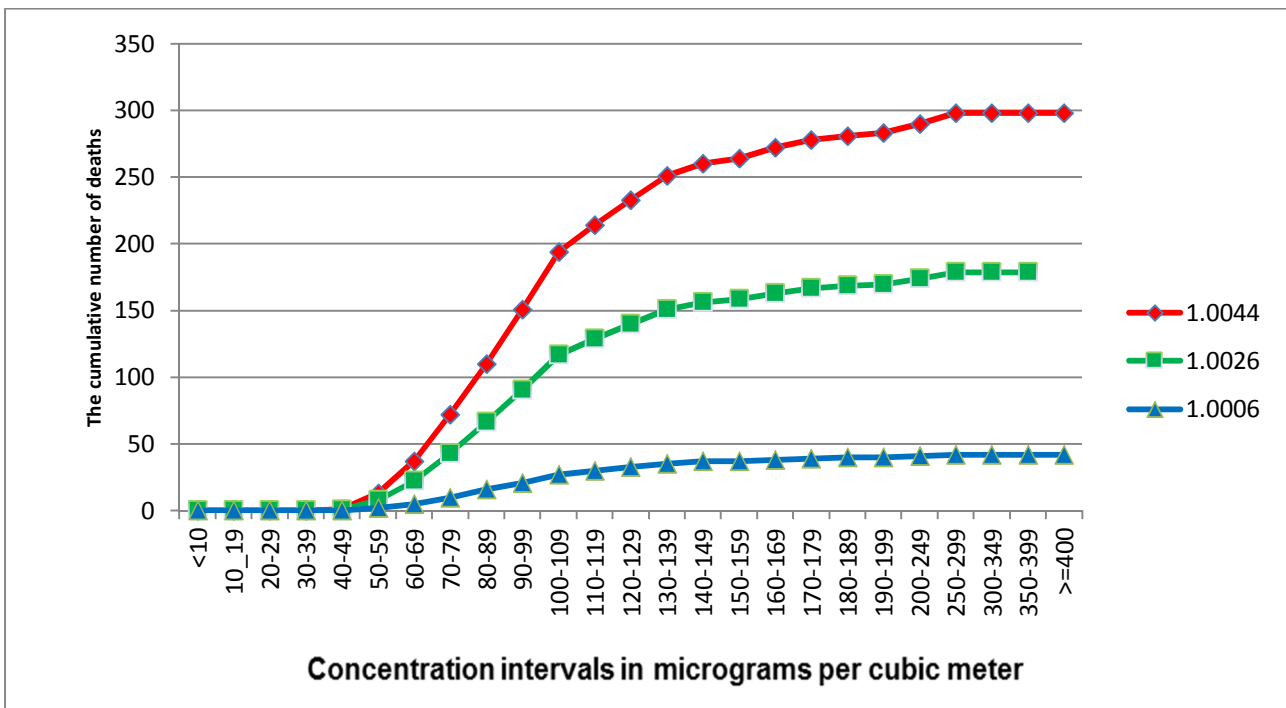


**Graph 1:** Cumulative cases of death from the NO<sub>2</sub> against concentration intervals in 2005

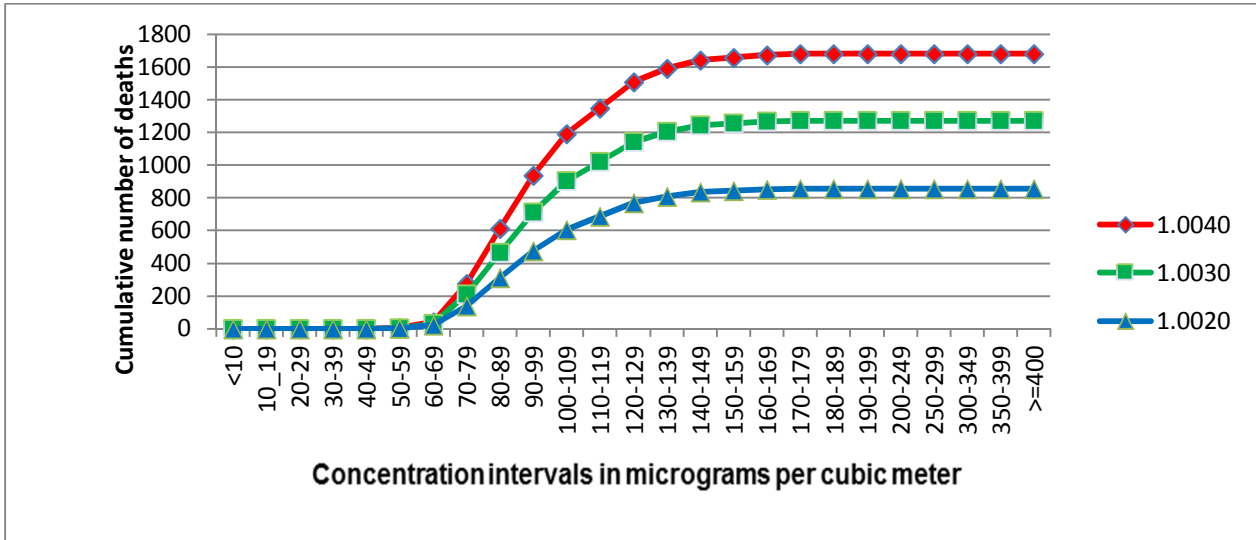
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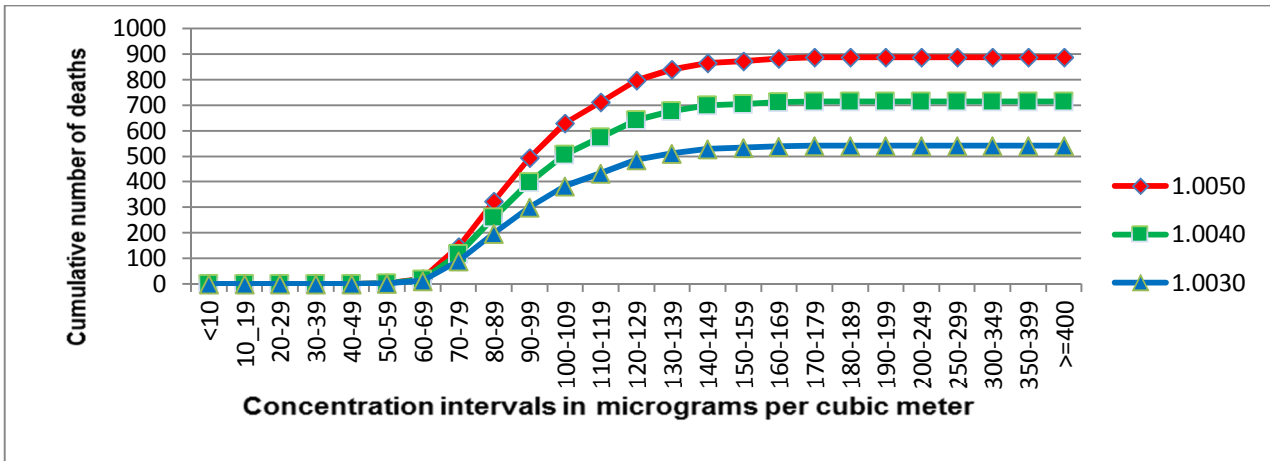
**Graph 2.** Cumulative number of cardiovascular mortalities caused by NO<sub>2</sub> against concentration intervals in 2005



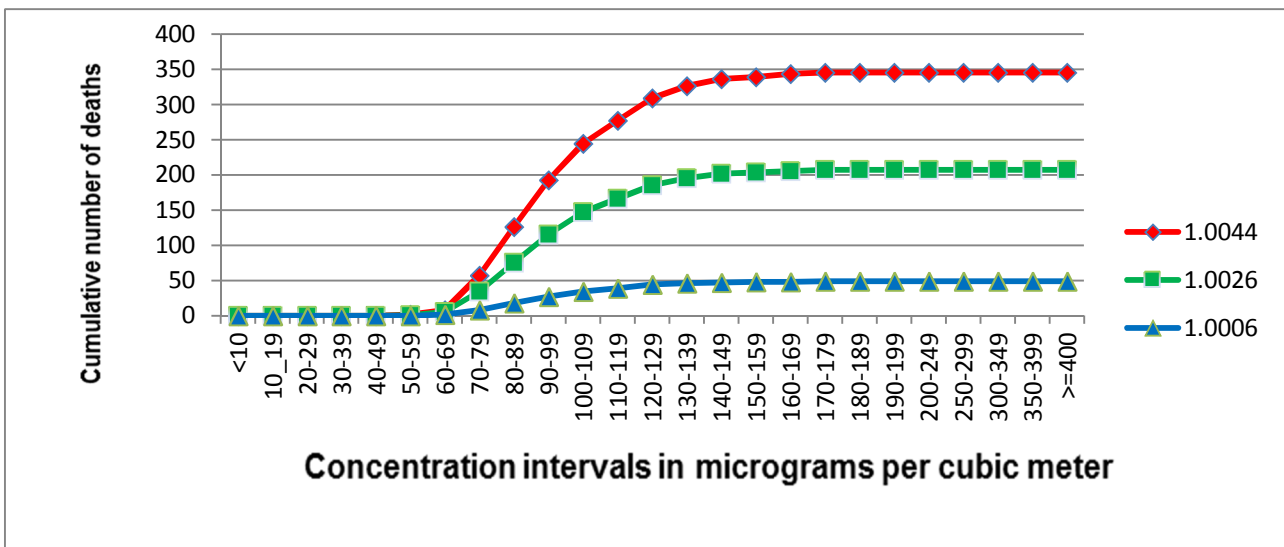
**Graph 3.** Cumulative number of hospitalization due to chronic obstructive pulmonary caused by NO<sub>2</sub> against concentration intervals in 2005



**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<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub>, O<sub>3</sub>, SO<sub>2</sub> 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<sub>2</sub> (29).

Goudarzi and his colleagues used AirQ model to assess the health effects of NO<sub>2</sub> in Tehran in 2008 and reported that the concentrations of NO<sub>2</sub> 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<sub>2</sub> and the daily mortalities (31). The results indicate the adverse effects of NO<sub>2</sub> on health. A single pollutant can act as an indicator of a pollutant mixtures. NO<sub>2</sub> 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<sub>2</sub>.

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.

## References

1. Bahrami Asl F, Kermani M, Aghaei M, Karimzadeh S, Salahshour Arian S, Shahsavani A, et al. Estimation of Diseases and Mortality Attributed to NO<sub>2</sub> pollutant in five metropolises of Iran using AirQ model in 2011-2012. *J Mazandaran Univ Med Sci* 2015;24(121):239-49. (Persian)
2. Fallah jokandan S, Kermani M, Aghaei M, Dolati M. Estimation the Number of Mortality due to cardiovascular and respiratory disease, Attributed to pollutants O<sub>3</sub>, and NO<sub>2</sub> in the Air of Tehran. *J Health Res Community* 2016;1(4):1-11. (Persian)
3. kermani m, aghaei m, bahramiasl f, gholami m, Fallah jokandan S, dolati m, et al. Estimation of cardiovascular death, myocardial infarction and chronic obstructive pulmonary disease (COPD) attributed to SO<sub>2</sub> exposure in six industrialized metropolises of Iran. *Razi J Medical Sciences*. 2016;23(145):12-21. (Persian)
4. Kermani M, Aghaei M, Gholami M, Bahrami asl F, Karimzade SA, Falah S, et al. Estimation of Mortality Attributed to PM<sub>2.5</sub> and CO Exposure in eight industrialized cities of Iran during 2011. *Iran Occup Health J* 2016;13(4):52-61. (Persian)
5. kermani M, dowlati M, A JONIDI JAFARI A, A REZAEI R. Study the number of cases cardiovascular mortality

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Attributed to CO in Tehran in during a five-year. *Rahavard Salamat J* 2016;2(3):38-47. (Persian)

6. Chaaban F. Air quality. In: Tolba MK and SaabNW, Editor Arab environment: future challenges. Technical Publications and Environment & Development Magazine. 2008:45-62.
7. Larsen B, others. Cost assessment of environmental degradation in the Middle East and north Africa region: selected issues. Economic Research Forum, working paper [Internet] 2011 [cited 2017 Jul 13]. Available from: <http://erf.org.eg/wp-content/uploads/2014/08/583.pdf>
8. Wark K WC, Davis WT Air pollution Its origin and control. New York: Addison Wesley Longman Press; 1998.
9. Younusian M. Air pollution epidemiology, studies and the ahead challenges science and health. The Sixth National Epidemiology Conference, Tehran: 2010. p. 34–5. (Persian)
10. Kermani M, Dowlati M, Jonidi Jafari A, Rezaei Kalantari R, Sadat Sakhaei F. Effect of Air Pollution on the Emergency Admissions of Cardiovascular and Respiratory Patients, Using the Air Quality Model: A Study in Tehran, 2005-2014. *Health in Emergencies and Disasters Quarterly* 2016;1(3):137–46.

11. Kermani M, Dowlati M, Jonidi Jafari A, Rezaei Kalantari R. Estimation of Mortality, Acute Myocardial Infarction and Chronic Obstructive Pulmonary Disease due to Exposure to O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> in Ambient Air in Tehran. *J Mazandaran Univ Med Sci* 2016;26(138):96-107. (Persian)
12. Kermani M, Dowlati M, jonidi jaffari A, Rezaei kalantari R. A Study on the Comparative Investigation of Air Quality Health Index (AQHI) and its application in Tehran as a Megacity since 2007 to 2014. *J Res Environ Health* 2016;1(4):275-84. (Persian)
13. kermani m, Dowlati M, Jonidi Jaffari A, Rezaei Kalantari R. Comparative Investigation of air quality Health in Tehran metropolis based on air quality index over a period of five years (2011-2015). *J Health Res Community* 2016;2(1):28-36. (Persian)
14. Kermani M, Jokandan SF, Aghaei M, Asl FB, Karimzadeh S, Dowlati M, et al. Estimation of the Number of Excess Hospitalizations Attributed to Sulfur Dioxide in Six Major Cities of Iran. *Health Scope* 2016;5(4).
15. Kermani M, fallah jokandan s, Aghaei M, dowlati M. Estimation of cardiovascular death, myocardial infarction and chronic obstructive pulmonary disease (COPD) attributed to PM and SO<sub>2</sub> in the air of Tehran metropolis. *J Res Environ Health* 2016;2(2):116-26. (Persian)
16. Kermani M, A Aghaei M, A Gholami M, A Bahrami asl F, A Karimzade S, A Falah S, et al. Estimation of Mortality Attributed to PM<sub>2.5</sub> and CO Exposure in eight industrialized cities of Iran during 2011. *Iran Occup Health J* 2016;13(4):52-61. (Persian)
17. Motesaddi Zarandi S, Raei Shaktaie H, Yazdani Cheratee J, Hosseinzade F, Dowlati M. Evaluation of PM<sub>2.5</sub> Concentration and Determinant Parameters on its Distribution in Tehran's Metro System in 2012. *J Mazandaran Univ Med Sci* 2013;22(2):37-46. (Persian)
18. Gryparis A, Forsberg B, Katsouyanni K, Analitis A, Touloumi G, Schwartz J, et al. Acute Effects of Ozone on Mortality from the "Air Pollution and Health. *Am J Respir Crit Care Med* 2004;170(10):1080-7.
19. Katsouyanni K, Touloumi G, Spix C, Schwartz J, Balducci F, Medina S, et al. Short-term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. *Air Pollution and Health: a European Approach. BMJ* 1997;314(7095):1658-63.
20. Schwartz J. Air pollution and hospital admissions for cardiovascular disease in Tucson. *Epidemiology* 1997;8(4):371-7.
21. Kelly FJ, Blomberg A, Frew A, Holgate ST, Sandstrom T. Antioxidant kinetics in lung lavage fluid following exposure of humans to nitrogen dioxide. *Am J Respir Crit Care Med* 1996;154(6):1700-5.
22. Hatami H. Integrated book of public health. Tehran: Arjmand publications; 2005. (Persian)
23. Folinsbee L. Does nitrogen dioxide exposure increase airways responsiveness? *Toxicol Ind Health* 1991;8(5):273-83.
24. Morrow PE, Utell MJ, Bauer MA, Smeglin AM, Frampton MW, Cox C, et al. Pulmonary performance of elderly normal subjects and subjects with chronic obstructive pulmonary disease exposed to 0.3 ppm nitrogen dioxide. *Am J Respir Crit Care Med* 1992;145(2):291-300.
25. WHO. Quantification of health effects of exposure to air pollution: report on a WHO working group, Bilthoven, Netherlands 20-22 November 2000. 2001 [cited 2017 Jul 13]; Available from: <http://apps.who.int/iris/handle/10665/108463>.
26. Gholampour A, Nabizadeh R, Naseri S, Yunesian M, Taghipour H, Rastkari N, et al. Exposure and health impacts of outdoor particulate matter in two urban and industrialized area of Tabriz, Iran. *J Environ Health Sci Eng* 2014;12:27.
27. Naddafi K, Hassanvand MS, Yunesian M, Momeniha F, Nabizadeh R, Faridi S, et al. Health impact assessment of

- air pollution in megacity of Tehran, Iran. *Iran J Environ Health Sci Eng* 2012;9(1):28.
28. Ghanbari Ghozikali M, Heibati B, Naddafi K, Kloog I, Oliveri Conti G, Polosa R, et al. Evaluation of Chronic Obstructive Pulmonary Disease (COPD) attributed to atmospheric O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> using Air Q Model (2011-2012 year). *Environ Res* 2016;144(Pt A):99-105.
29. Burnett RT, Smith-Doiron M, Stieb D, Cakmak S, Brook JR. Effects of particulate and gaseous air pollution on cardiorespiratory hospitalizations. *Archives of Environmental Health: An Int J* 1999;54(2):130-9.
30. Goudarzi G, Naddafi K, Mesdaghinia A. Quantifying the health effects of air pollution in Tehran and determination of the third axis Integrated program effects to reduce the effect of air pollution in Tehran. (Dissertation). Tehran: Tehran University of Medical Sciences; 2009. (Persian)
31. Touloumi G, Katsouyanni K, Zmirou D, Schwartz J, Spix C, de Leon AP, et al. Short-term effects of ambient oxidant exposure on mortality: a combined analysis within the APHEA project. *Am J Epidemiol* 1997;146(2):177-85.