Evaluation of Chronic Obstructive Pulmonary Disease Attributed to Atmospheric O_3, NO_2 and SO_2 in Tehran City, from 2005 to 2014

Majid Kermani[1,2], Ahmad Jonidi Jafari [1,3], Roshanak Rezaei kalantari [1,3], Fazeleh Sadat Sakhaet [4], Tannaz Sadat Kahe [4], Mohsen Dowlati [*1]

1) Department of Environmental Health Engineering, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
2) Research Center for Environmental Health Technology, Iran University of Medical Sciences, Tehran, Iran.
3) Department of Environmental Health Engineering, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
4) School of Nursing, Iran University of Medical Sciences, Tehran, Iran.

** Author for Correspondence: mohsendowlati.69@gmail.com*

Received: 07 Dec. 2016, Revised: 08 Feb. 2017, Accepted: 4 Feb. 2017

ABSTRACT
Air pollution in Tehran is considered as one of the most important factors threatening human health. High concentrations of pollutants have adverse effects on citizens and the environment. We calculated the relation between COPD and criteria air pollutants in Tehran, one of the most polluted cities in the world during 2005 to 2014.
Hourly data of pollutants include SO_2, O_3 and NO_2 were taken from the Tehran environmental protection agency and Air Quality Control Company. The AirQ2,2,3 model that proposed by the WHO, is used to health impact assessment of pollutants in terms of hospital admission due to Chronic Obstructive Pulmonary Disease. Results indicated that the total cumulative number of cases due to hospital admission due to COPD in Tehran city from 2005 to 2014 for SO_2, O_3 and NO_2 was 1806, 2941 and 2454 cases, respectively. The finding of this study showed that total mean of SO_2, O_3 and NO_2 was higher than the standard concentration. By comparison with guideline and standards, annual concentration for SO_2, O_3 and NO_2 was exceeded on standard level in during the study period.
This study demonstrated that a high percentage of hospital admission due to Chronic Obstructive Pulmonary Disease resulting from these pollutants could be due to the high average concentration in the air of Tehran during 2005 to 2014. So, authorities must apply the efforts and necessities actions based on comprehensive scientific researches to control air pollutants and abate their negative effects on human health.
Key words: Air Pollution; Atmospheric Pollutants; Environment; Chronic Obstructive Pulmonary Disease; Health Impact

INTRODUCTION
Air pollution in Tehran is one of the health and environmental problems in many large cities of the world such as Tehran. Researches over the last two decades have determined that there is a direct relationship between air pollution and health of people [1-5]. Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory airway disease that described by hypersecretion, cough and inflammatory cell influx and persistent airflow limitation [6,7]. According to the prediction and estimation of the World Health Organization, about 80 million people have gotten moderate to severe COPD and 3 million people of them died of COPD in 2005, which corresponds almost 5% of all deaths globally. Total deaths due to COPD are projected to increase by more than 30% in the next 10 years [8]. By the year 2020, it has been estimated that COPD will rank 5th among the conditions with a high burden to society [9]. The gaseous pollutants such as ozone (O_3), nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) are highly reactive oxidants and can cause COPD at high concentrations. Ozone is a pollutant which can cause respiratory and cardiovascular diseases, eye burning sensation and failure of immune defense against infectious diseases. The following formula represents the ozone formation on the surface of earth (lower layer of troposphere) [10].

$$\mathbf{VOC+NO_X+Heat+Sunlight \rightarrow O_3}$$

In general, ozone enters the body as the following explanation: The membranes are made of both proteins and lipids; therefore, they are the proper aims for the ozone attack. Researches on human and animals demonstrated that some pulmonary disorders and complications are caused by the ozone exposure. United States National Ambient Air Quality Standards have appointed 0.075 ppm as the highest daily maximum 8- hour ozone concentrations [11-13]. The ozone effects as follows:
1- Histological changes in bronchiolar epithelium when it is in long -term exposure to O_3 concentrations of 1 to 0.2 ppm.

2- Changes in lungs function in communication with ozone concentrations of 0.3 ppm for two hours which is reversible after discontinuation of the contact.
3- Changes in the lungs protein structure after one hour of contact with ozone.
4- Creation Biochemical changes of lungs and another limbs after four hours of contact with ozone concentrations of 3 to 6 ppm.
5- Increased capacity to bacterial infections in a three- hour impact with ozone concentration of 0.8 ppm.
6- Effect on expiratory volume [14-16]. Nitrogen dioxide (NO_2) is a by-product of high-temperature fossil fuel combustion. It is a ubiquitous pollutant in urban environments as well as indoor environments coming from combustion sources [17]. NO_2 also is an important marker of air quality. A recent review provided moderate evidence that long-term exposure to an annual mean concentration below 40 μg/m^3 of this pollutant was correlated with harmful health effects such as respiratory diseases, hospital admissions and mortality [18]. Human activities represent the main sources of NO_2, from automobile exhaust emissions to stationary sources such as fossil fuels, power plants, industrial boilers, waste incinerators and heating household devices; but the main source of nitrogen dioxide in the air is the gas emitted by the public transportations. NO_2 concentration varies from morning to night. The main sources of NO_2 in the indoor environment are the natural gas primus and the smoke created by cigarettes. Acute short-term (one hour) effects and low concentrations have been observed in animals [19-21]. Sulfur dioxide is a colorless gas that released from burning of coal and diesel fuel. SO_2 and particulates together form a major portion of the pollutant load in many cities. SO_2 may cause irritation, decrease of visibility and some respiratory illness. Healthy personal experience branch construction at 1.6 ppm of SO_2, for a very few minutes exposure at 8-12 ppm level throat irritation occurs. At 20 ppm, immediate cough and eye irritation happen. Even for exposure of SO_2 at 400-500 ppm is dangerous for life. Sulfur dioxide (SO_2) harms human health by reacting with the humidity in the nose, nasal perforation and throat and this is the way in which it annihilate the nerves in the respiratory system present. When the concentration of SO_2 is higher than the prescribed standards of the World Health Organization (WHO), it effects especially on those suffering from asthma, bronchitis, lung and cardiac problems [22]. Many of studies performed about air pollution in Tehran city that demonstrated high concentration for SO_2, O_3 and NO_2. In study of Naddafi *et al.* annual average for SO_2, O_3 and NO_2 in 2011-2012 89, 85 and 68 μg/m^3 were estimated. A large number of studies show that acute and chronic morbidity such as COPD are due to gaseous air pollutants. In a study by Gharechahi *et al.* , there was significant relationship between sulfur dioxide and hospital admission due to respiratory diseases in elderly group and COPDs ($p< 0.001$) [23]. Also Stieb *et al.*. (2009) showed how an increase of 18.4 ppb level of O_3 concentration was associated with an increase of emergency room visits for COPD 3.7%(95%CI: 0.5% to7.9%) [24]. Tehran is a developed and industrialized city of Iran, with about 450,000 people population. Its longitude and latitude are 51°25 E and 35°34 N respectively and its elevation is about 1000–1800 meters above sea level. Tehran is located in valleys and is surrounded on the north, northwest, east and southeast by high to medium (3800–1000 m) mountain ranges. The mountain range pauses the flow of the moist wind to the capital and prevents the air pollution from being carried away from the city. Thus, during winter, lack of wind and cold air causes the polluted air to be trapped within the city [25]. These concomitant conditions make Tehran one of the worst regions in the world for atmospheric pollution for many days exceeding air quality standards during each year [26]. As health endpoints in Tehran during a period of ten years has not been Evaluated. Therefore, the present study is aimed to evaluate Chronic Obstructive Pulmonary Disease (COPD) attributed to atmospheric O_3, NO_2, and SO_2 in Tehran City, during 2005-2014 year.

MATERIALS AND METHODS

This study was a descriptive–analytic and AirQ 2.2.3 software were used to Evaluation of Chronic Obstructive Pulmonary Disease (COPD) attributed to atmospheric O_3, NO_2, and SO_2 in Tehran city. Location of Tehran is shown in Fig. 1.
Hourly data of pollutants were collected from Tehran environmental protection agency and Air Quality Control Company. These data were on volumetric base, but AirQ software has been designed on gravimetric base, so we obtain data of pressure and temperature from I.R. of Iran meteorological organization and use following equation to convert ppb unit (DOE data) to μg/m^3 unit (model required):

$$\frac{\mu g}{m^3} = \frac{P\,(mmHg) \times MW \times ppm}{62.4 \times T\,(°K)} \times 1000 \qquad (1)$$

MW Is molecular weight of pollutant, T is temperature as Kelvin degree and P is pressure.

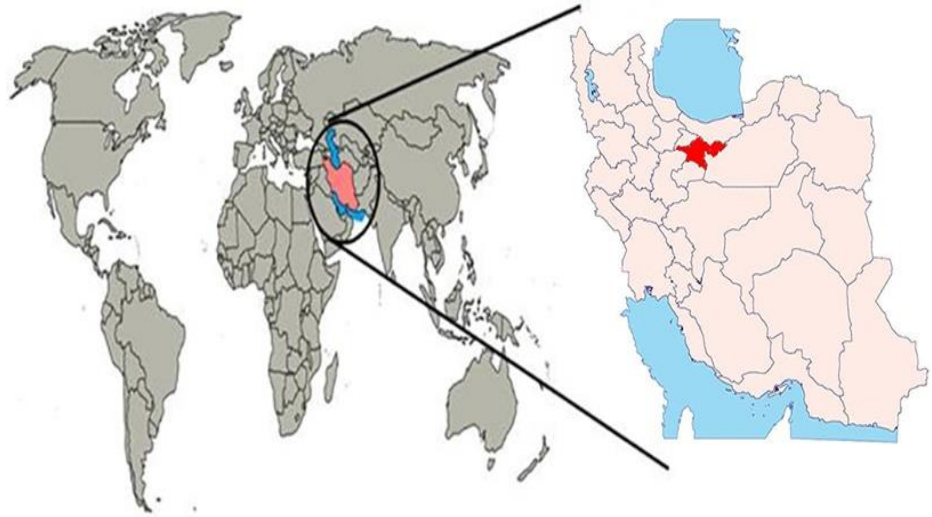


Fig. 1: Map of Iran in the world and location of studied City (Tehran megacity)

To determine the data validity for performing statistical analyzes, based on WHO criteria, the data recorded at weather stations were subjected to primary and secondary processing. In the primary processing, the exclusion of unnecessary data, sheet layout of the pollutants, and time standardization (to provide the median estimate) were performed and on the basis of WHO criteria, the number of weather stations with valid data were identified. In this regard, the ratio between the number of valid data for the 2 seasons (warm and cold season) should not be more than 2. Also, in order to achieve the median 24 hour values, at least 50% data must exist with sufficient validity.

For health impact quantification due to exposure with $_{SO2}$, annual mean, winter and summer mean, annual 98 percentile, annual maximum and winter and summer maximum was calculated in all years. All of these corrections, processing and required statistical parameters calculation were performed by using Microsoft Office Excel spread sheet. For all the pollutants, the parameters required by the software (annual and seasonal average, maximum and annual98th percentiles) were calculated. Hospital admission due to (COPD) related to O_3, NO_2, and SO_2 by AirQ2.2.3 tool. AirQ 2.2.3 software was introduced by the WHO in 2004 and developed by the WHO European Center for Environment and Health, Bilthoven Division. This model is used to estimate the impacts of exposure to specific air pollutants on the health of people living in a certain period and area. The assessment is based on the attributable proportion (AP), defined as the fraction of the health outcome in a certain attributable population expose to a given atmospheric pollutant [27]. The AP can be calculated by the following equation

$$\text{AP=SUM }\{[RR(c)-1]\times p(c)\}/\text{SUM }[RR(c)\times p(c)] \quad (2)$$

P(c) is the population of city and RR is the relative risk of health endpoints in category "C" of exposure that obtain from epidemiological study and exposure-response functions.

Relative Risk (RR) is defined as a ratio of the probability of the event when people exposure to probability of the event when people non-exposed. Rate of the health outcome attributable to the exposure (IE), calculated as follows:

$$IE=I\times AP \quad (3)$$

Where, (I) is the baseline frequency of the health outcome in the population under investigation (survey). Number of cases attributable to the exposure to pollutant (NE) with knowing size of population (N) can be calculated as following:

$$NE=IE\times N \quad (4)$$

Baseline incidence (BI) multiplied at population size and Attributable proportion (AP) then divided to 10^5 to obtain number of excess cases:

$$\left(\frac{\textbf{Baseline incidence}\times\textbf{ Population}}{\mathbf{10^5}}\right)\times\textbf{Attributable proportion}=\textbf{No. of excess cases} \quad (5)$$

Finally after importing prepared data to AirQ 2.2.3 Software, results present as the excess cases of hospital admission due to chronic obstructive pulmonary disease (COPD) attributed to Ozone (O_3), Nitrogen dioxide (NO_2) and Sulfur dioxide (SO_2) pollutant in ten years.

RESULTS AAND DISCUSSIONS

The Annual concentrations of pollutants

The annual average maximum, summer average, winter average, and 98 percentiles of O_3, NO_2 and SO_2 concentrations have been showed in Table 1. As can be seen in Table 2, among the-ten studied years, highest annual concentration of sulfur dioxide

($\mu g/m^3$) was reported in year 2008 and 2007, with mean value of 112 and 89 $\mu g/m^3$, respectively. Iran national standards set and determined 20$\mu g/m^3$ for annual mean of SO_2, and according to these standards, all of the studied years exceeded by the national standard. During the study period of 2005-2014, annual mean concentration of SO_2 was 2.22, 4.32, 4.49, 5.63, 4.13, 4.07, 2.98, 2.58, 2.02 and 1.96 times higher than national standards, respectively (Fig.2). For nitrogen dioxide highest annual concentration ($\mu g/m^3$) was reported in year 2008 and 2007, with mean value of 205 and 166 $\mu g/m^3$, respectively. WHO guideline [28] set and determined 40$\mu g/m^3$ for annual mean of NO_2, that according to these standards, all of the studied years exceeded from national standard. During the study period, in 2005-2014, annual mean concentration of NO_2 was 2.37, 2.72, 4.15, 5.13, 3.15, 3.28, 2.32, 2.15, 2.52 and 2.4 times higher than standards, respectively (Fig.2). According to the table1 annual mean concentration of pollutants in 2008 to 2014 has a decreasing slope. This may be due to the reduction of sulfur in the fuel and increase of transport that use compressed natural gas (CNG) for gas up—albeit this point has been confirmed by Department of Environment (DOE) that those vehicles that use gasoline for gas up are responsible for SO_2 pollution. Also these trends could be related to the control program (entering of new equipped vehicles with better fueling devices, using catalytic transformer in new vehicles and devices, and having compulsory standards of Euro 1 and 2 for under-constructing ones). In spite of increased levels of NO_2 concentration, very low development was seen. Although, supervising plan in Tehran city was considered to use engines with better combustion and produce fewer NO_2, and decreasing emission of NO_2 per mile study of Motesaddi Zarandi *et al.* On Long-term trends of Nitrogen oxides and surface ozone concentrations in Tehran city, 2002–2011confirm this finding [29]. Due to the large number of charts in ten years we preferred to show last year studied (2014) in Fig. 2. Fig 2 shows the percentage of time people in Tehran was exposed to different concentrations of pollutants during 2014.

The highest number of days of exposure to NO_2 in 2014 was observed in the concentration category of 80–89 and 90–99 $\mu g/m^3$ which was higher than NAAQSs published standards for annual mean NO_2. Also, the highest numbers of days of exposure to SO_2 and O_3 concentrations were in the concentration range of 30–39, 40–09 and 70–79 $\mu g/m^3$ in 21 March 2014 to 20 March 2015.

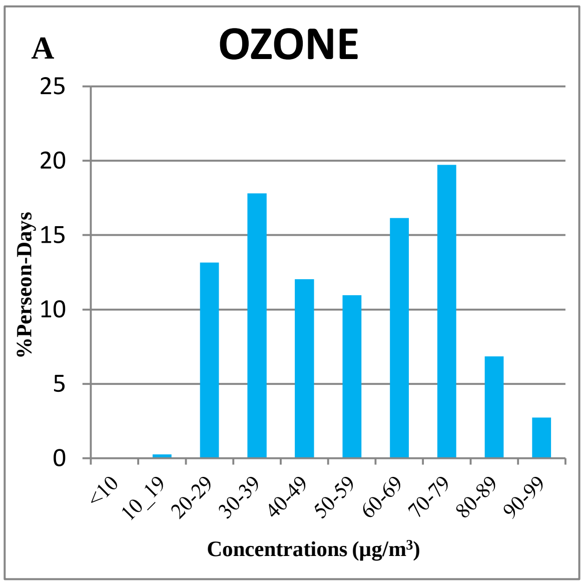
The baseline incidence and relative risks

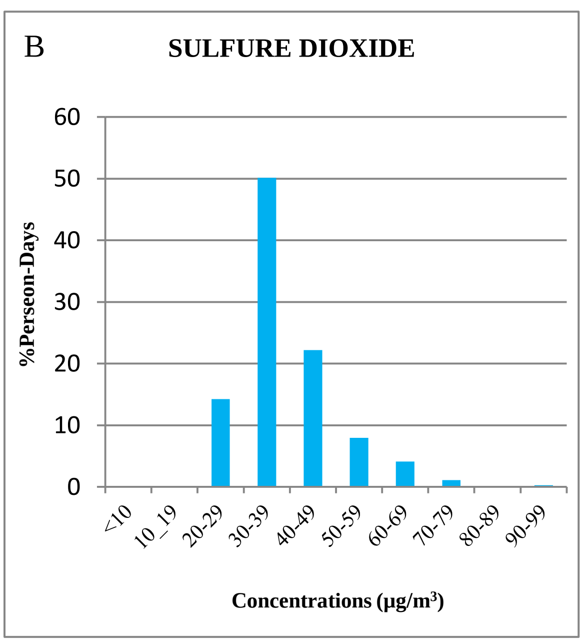
Cases of Hospital admissions due to chronic obstructive pulmonary disease (COPD) attribute to expose with SO_2, O_3, and NO2 Was estimated by AirQ2.2.3 model in ten years in Tehran. Baseline incidence (BI) and relative risks with 95% confidence intervals (95% CI) that used for the health effect estimation in present study are shown in table 2. Relative risks and BI used in this study based on other studies conducted in Iran [25,30] and compared with that of World Bank [31] and World health statistics 2013 [32] to make sure for accuracy and precision. The average BI was about 5 per1000 people for Iran due to having young population. According to the results of table 2, with increasing each 10 $\mu g/m^3$ concentration of SO_2, O_3, NO_2, risk of HA-COPD increased 0.44% (1 per CI= 0.05 and 1.01 per CI= 0.95), 0.58% (1.0022 per CI= 0.05 and 1.0094 per CI= 0.95) and 0.64% (1.0006 per CI= 0.05 and 1.0044per CI= 0.95) respectively. Indicators of relative risk (RR) and Attributable Proportion (AP) for COPD to NO_2 is defined on base- line Incidence (BI) 101.4 at 10^5 persons by the WHO.

Cases of hospital admission du exposure to SO_2, O_3, NO_2 pollutants

Number of excess cases of hospital admission due to COPD due to short-term exposure above 10$\mu g/m^3$ for SO_2, O_3, and NO_2 in ten years estimated that showed in Table 3. Results showed, total cumulative number of cases due to HA-COPD estimated in the present study for ten years SO_2, O_3 and NO_2 was 1806, 2941 and 2454 cases in central RR in a year, respectively. As seen in table 4, with regard to AP and exposed population, maximum number of extra hospital admission due to COPD for NO_2 among investigated years belonged to the year 2008 with 388 cases. Also maximum number of excess hospital admission due to COPD for O_3 among investigated years belonged to 2008 with 414 cases. Finally maximum number of excess hospital admission due to COPD for SO_2 among investigated years belonged to the year 2007 with 293 cases. Results the study conducted in Tehran by Naddafi and *et al.* [25] showed number of excess cases attributed to NO_2, SO_2, and O_3 in with percentage of attributable proportion (AP) 2.79, 3.38 and 4.80, was 247, 298 and 424 cases respectively. Ghanbari and *et al.* studied quantification of the health effect of COPD from exposure to NO_2, SO_2, and O_3 in Tabriz in 2009 [33] and results of this study showed that attributable proportion, and number of persons suffering from COPD due to O_3, NO_2, and SO_2 exposure (BI=101.4 per105 persons) was 2.9%, 0.89%, 0.41%, 44, 13 and 6 cases, respectively. The results of both studies are somewhat close together in metropolitan of Tabriz is very similar with and this study in mega city of Tehran, Iran. The results of another study in Europe, the APHEA project (a Meta centric and multi-pollutant study) evaluated air pollution (multi-pollutant) and its short-term effects such as HACOPD. The RR for a 50 $\mu g/m^3$ in-crease in the daily mean level of pollutant was 1.02 (95%CI0.98–1.06) for SO_2, 1.02(95%CI1.00–1.05) for NO_2 and 1.04 (95%CI1.02– 1.07) [25]. Other studies have been conducted in US cities, by Medina-

Ramón *et al.* (2006) (41) European cities, by Anderson *et al.* (1997) [35] Milan (Italy) Fattore *et al.* (2011) [34] and Hong Kong (China) Ko *et al.* [36]. On the health effects of atmospheric pollution, as this study has confirmed, they found there is association between gausses pollutants (O_3, NO_2 and SO_2) and HA COPD, as well. Totally researches carried out in this issue showed convincing evidences from the role of pollutants in the incidence of COPD. In fact, various factors, such as smoking, occupational exposures, inappropriate diet, indoor air pollution, exposure to SO_2, O_3, and NO_2 can influence incidence of COPDs, especially in elderly people, but exposure to air pollutants can exacerbate these diseases as predisposing factors [23].





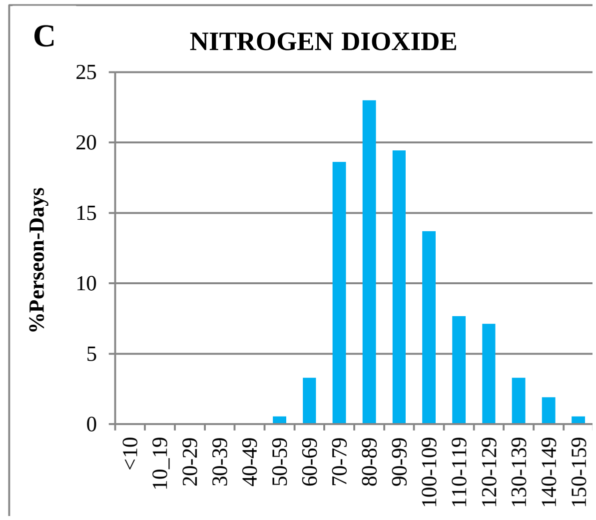
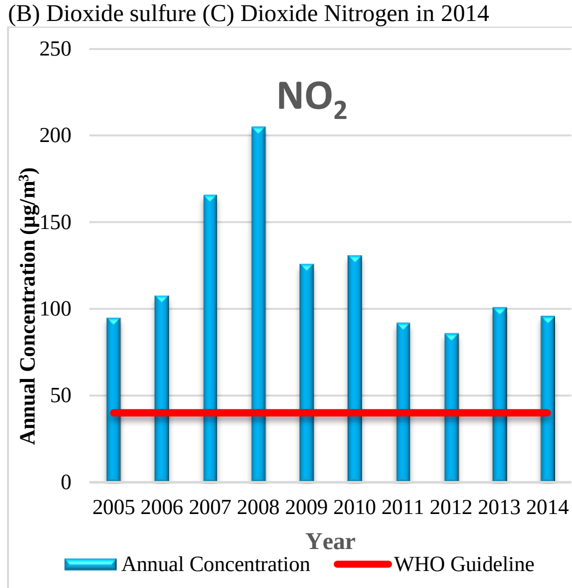


Fig.2: Percentage of days that people in Tehran were exposed to different concentrations of pollutants (A) Ozone (B) Dioxide sulfure (C) Dioxide Nitrogen in 2014



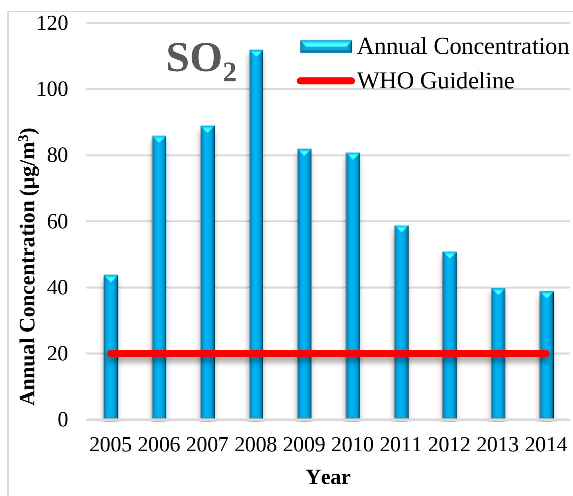


Fig. 3: Compare of annual mean concentration of NO_2 and SO_2 with WHO Guideline

Table 1. Summary of required statistical parameters, O_3, NO_2, SO_2, ($\mu g/m^3$) by means of the model (Tehran, Iran, 2005-2014)

Year	Pollutant	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Average annual	NO_2	95	108	166	205	126	131	92	86	101	96
	SO_2	44	86	89	112	82	81	59	51	40	39
	O_3	50	51	69	96	86	74	63	64	63	55
Average summer	NO_2	90	109	132	174	119	117	89	86	92	88
	SO_2	39	59	49	122	64	78	51	48	37	35
	O_3	59	65	85	118	113	100	78	83	76	71
Average winter	NO_2	100	108	201	237	133	145	96	85	110	104
	SO_2	49	114	131	102	101	85	67	54	43	43
	O_3	40	35	52	74	59	47	48	44	49	37
98 percentiles annual	NO_2	196	174	322	450	183	208	139	119	156	143
	SO_2	101	213	208	207	146	165	95	75	68	68
	O_3	81	114	119	174	154	143	122	105	107	93
Maximum annual	NO_2	261	356	386	644	297	228	218	122	197	174
	SO_2	123	330	258	312	181	219	110	90	81	94
	O_3	110	139	131	206	250	164	163	126	154	76
Maximum summer	NO_2	173	178	213	334	183	208	218	121	137	128
	SO_2	59	118	85	206	103	121	84	67	54	53
	O_3	110	139	131	206	250	164	154	111	123	102
Maximum winter	NO_2	261	356	386	644	297	228	173	122	197	174
	SO_2	123	330	258	312	181	219	110	90	81	94
	O_3	73	113	106	144	116	91	163	126	154	76

Table 2: Baseline incidence and relative risks for HA- COPD of SO_2, O_3, NO_2 in this study

Pollutant	Baseline incidence	RR (95% CI) per 10 $\mu g/m^3$
NO_2		1.0026(1.0006-1.0044)
SO_2	101.4	1.0044 (1–1.011)
O_3		1.0058(1.0022-1.0094)

Table 3: Number of cases Hospital admission and attributable proportion due to COPD in Tehran city, during 2005-2014

Health end point (hospitalization)	Year	Pollutant	AP (attributable proportion)	No. of excess cases (uncertainty range)
ospital admission due to chronic obstructive pulmonary (HA- COPD)	2005	NO_2	2.17 (0.51-3.62)	178 (41-297)
		SO_2	1.47 (0- 3.61)	121 (0-297)
		O_3	2.27 (0.87-3.62)	186 (71-298)
	2006	NO_2	2.52 (0.59-4.19)	212 (50-353)
		SO_2	3.02 (0- 7.23)	255 (0-610)
		O_3	3.39 (1.76-5.04)	286 (149-425)
	2007	NO_2	4.02 (0.95-6.62)	344 (82-566)
		SO_2	3.46 (0- 8.17)	293 (0-698)
		O_3	3.34 (1.29-5.3)	285 (110-453)
	2008	NO_2	4.6 (1.10-7.55)	399 (95-655)
		SO_2	1.35 (0- 3.32)	117 (0-288)
		O_3	4.78 (1.86-7.52)	414 (162-652)
	2009	NO_2	2.92 (0.69-4.85)	257 (60-427)
		SO_2	3.13 (0- 7.48)	276 (0-660)
		O_3	4.29 (1.67-6.77)	377 (147-596)
	2010	NO_2	3.08 (0.73-5.11)	275 (65-456)
		SO_2	1.67 (0- 3.91)	143 (0-349)
		O_3	3.59 (1.39-5.7)	321 (124-509)
	2011	NO_2	2.10 (0.49-3.51)	190 (44-318)
		SO_2	2.13 (0- 5.16)	193 (0-467)
		O_3	3.02 (1.16-4.81)	273 (105-435)
	2012	NO_2	1.94 (0.45-3.24)	178 (41-297)
		SO_2	1.8 (0- 4.39)	166 (0-403)
		O_3	3.06 (1.18-4.87)	281 (108-447)
	2013	NO_2	2.31 (0.54-3.85)	215 (50-359)
		SO_2	1.32 (0- 3.24)	123 (0-302)
		O_3	2.98 (1.15-4.75)	278 (107-442)
	2014	NO_2	2.18 (0.51-3.64)	206 (48-344)
		SO_2	1.26 (0- 3.11)	119 (0-294)
		O_3	2.54 (0.98-4.06)	240 (92-383)

CONCLUSIONS

This study was the first survey to assess health impacts of air pollution in Tehran, Iran in the recent decade period year 2005 to 2014. Although the results of this study are in line with results from other studies, since the climate, demographic and geographic characteristics is different, there is still high need to further studies to specify local RRs and BIs instead of WHO defaults. According to WHO, COPD was estimated to be the 12th cause of disability and the sixth cause of mortality in 1990, and it is also estimated to be the 5th cause of disability and the third cause of mortality by 2020. Nitrogen dioxide, sulfur dioxide, and ozone has a significant impact on COPD hospitalization. This study applied the AirQ software assesses the health impact of air pollution for citizenship in Tehran, one of the most populated areas in the world, where the geographical features make the air quality among the worst in the world. As presented in this study, air quality affects daily hospital admissions dramatically. So authorities must apply the management schemes and comprehensive measures based on comprehensive scientific researches Such as Restriction of use of fossil resources, improving public transportation systems, traffic management quality of the auto industry productions and, etc, to control air pollutants and diminishing the health impacts on human health. The results convince urban air pollution authorities and governmental decision makers to conflict for finding optimized model about to anthropogenic sources and reduce air pollution concentrations and/or reduce exposure of people to air pollutants.

ETHICAL ISSUES

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/ or falsification, double publication and/ or submission, redundancy, etc.) have been completely observed by the authors.

CONFLICT OF INTERSTS

All authors declare that they have no actual or potential competing financial interest.

AUTHORS' CONTRIBUTIONS

All authors read and approved the final manuscript.

FUNDING/SUPPORTING

The authors would like to thank the facility supported by Vice Chancellor for Research and Technology, Iran University of Medical Sciences.

ACKNOWLEDGEMENT

This work was funded by Iran University of Medical Sciences, Grant number 25455. We also thank environmental protection agency Tehran and Air Quality Control Company for providing us pollutants concentrations data. We acknowledge the critical comments from anonymous reviewers and editor.

REFERENCES

[1] 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 PM2.5 and CO Exposure in eight industrialized cities of Iran during 2011. Iran Occupational Health Journal. 2016;13(4):52-61.

[2] Kermani M, Dowlati M, Jonidi Ja`fari 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.

[3] 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_3, NO_2, and SO_2 in Ambient Air in Tehran. Journal of Mazandaran University of Medical Sciences. 2016;26(138):96-07.

[4] Kermani M, Fallah Jokandan S, Aghaei M, Bahrami Asl F, Karimzadeh S, Dowlati M. Estimation of the Number of Excess Hospitalizations Attributed to Sulfur Dioxide in Six Major Cities of Iran. Health Scope.Inpress(Inpress):e38736.

[5] Motesaddi Zarandi S, Raei Shaktaie H, Yazdani Cheratee J, Hosseinzade F, Dowlati M. Evaluation of PM2.5 Concentration and Determinant Parameters on its Distribution in Tehran's Metro System in 2012. Journal of Mazandaran University of Medical Sciences. 2013;22(2):37-46.

[6] Barnes PJ. Targeting Histone Deacetylases in Chronic Obstructive Pulmonary Disease. In: Roach IH, Bronner F, Oreffo OCR, editors. Epigenetic Aspects of Chronic Diseases. London: Springer London; 2011. 10(2): 205-15.

[7] Killian KJ, Leblanc P, Martin DH, Summers E, Jones NL, Campbell EJ. Exercise capacity and ventilatory, circulatory, and symptom limitation in patients with chronic airflow limitation. Am Rev Respir Dis. 1992;146(4):935-40.

[8] Liu Y, Lee K, Perez-Padilla R, Hudson NL, Mannino DM. Outdoor and indoor air pollution and COPD-related diseases in high- and low-income countries. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2008;12(2):115-27.

[9] Murray CJL, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. The Lancet. 1997;349(9064):1498-504.

[10] Izzotti A, Parodi S, Quaglia A, Farè C, Vercelli M. The relationship between urban airborne pollution and short-term mortality: Quantitative and qualitative aspects. European Journal of Epidemiology. 2000;16(11):1027-34.

[11] Gardner MW, Dorling SR. Neural network modelling and prediction of hourly NOx and NO_2 concentrations in urban air in London. Atmospheric Environment. 1999;33(5):709-19.

[12] Noori R HG, Ashrafi K, Nadjar-Araabi B. Uncertainty analysis of developed ANN and ANFIS models in prediction of carbon monoxide daily concentration. Atmos Environ 2010;44(4):476-82.

[13] Nunnari G, Dorling S, Schlink U, Cawley G, Foxall R, Chatterton T. Modelling SO_2 concentration at a point with statistical approaches. Environmental Modelling & Software. 2004;19(10):887-05.

[14] Cheremisinoff N. Handbook of Air Pollution Prevention and Control. New York: Elsevier; 2006.

[15] Heinsohn RJ KR. Sources and control of air pollution. New Jersey: Prentice Hall; 1998. 66-652 p.

[16] Colls J. Air pollution: measurement, modeling and mitigation. London: Spon Press 2206.

[17] Kampa M, Castanas E. Human health effects of air pollution. Environmental pollution (Barking, Essex : 1987). 2008;151(2):362-67.

[18] Latza U, Gerdes S, Baur X. Effects of nitrogen dioxide on human health: systematic review of experimental and epidemiological studies conducted between 2002 and 2006. International journal of hygiene and environmental health. 2009;212(3):271-87.

[19] Al-Hurban AEaA-O, A. N. Textural characteristics of dust fallout and potential effect on public health in Kuwait City and suburbs. Environmental Earth Sciences. 2010;60(1):169-18.

[20] Fung K, Krewski, D., Burnett, R. and Dominici, F. Testing the harvesting hypothesis by time-domain regression analysis. I: baseline analysis. Journal of Toxicology and Environmental Health, Part A, 68, pp. 2005;68:1137-54.

[21] Traversi D, Degan R, De Marco R, Gilli G, Pignata C, Ponzio M, *et al.* Mutagenic properties of PM2.5 air pollution in the Padana Plain (Italy) before and in the course of XX Winter Olympic Games of "Torino 2006". Environment international. 2008;34(7):966-70.

[22] Rahila Rahman Khan MJAS. Review on effects of Particulates; Sulfur Dioxide and Nitrogen Dioxide on Human Health. International Research Journal of Environment Sciences. 2014;3(4):70-73.

[23] Gharehchahi E, Mahvi AH, Amini H, Nabizadeh R, Akhlaghi AA, Shamsipour M, *et al.* Health impact assessment of air pollution in Shiraz, Iran: a two-part study. Journal of Environmental Health Science and Engineering. 2013;11:11. doi:10.1186/2052-336X-11-11

[24 Stieb DM, Szyszkowicz M, Rowe BH, Leech JA. Air pollution and emergency department visits for cardiac and respiratory conditions: a multi-city time-series analysis. Environmental health : a global access science source. 2009;8:25.

[25] 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. Iranian Journal of Environmental Health Science & Engineering. 2012;9(1):1-7.

[26] WHO. Urban outdoor air pollution database. Geneva, Switzerland: Department of Public Health and Environment, World Health Organization; 2011.

[27] Fattore E, Paiano V, Borgini A, Tittarelli A, Bertoldi M, Crosignani P, *et al.* Human health risk in relation to air quality in two municipalities in an industrialized area of Northern Italy. Environ Res. 2011;111(8):1321-27.

[28] WHO. Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide: Summary of risk assessment. Publications of the World Health Organization; 2005.

[29] Motesaddi Zarandi S, Alimohammadi M, Kazemi Moghaddam V, Hasanvand MS, Miranzadeh MB, Rabbani D, *et al.* Long-term trends of Nitrogen oxides and surface ozone concentrations in Tehran city, 2002–2011. Journal of Environmental Health Science and Engineering. 2015;13(1):1-6.

[30] 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.

[31] United Nations, Department of Economic and Social Affairs, Population Division, 2011. World Population Prospects: the 2010 Revision. www.un.org/population/.../WPP2010/WPP2010_Volume-I_ Comprehensive-Tables.pdf

[32] WHO. World health statistics Geneva, Switzerland 2013. available from: www.who.int/gho/world_health_statistics/EN_WHS2013_Full.pdf

[33] Ghozikali MG, Mosaferi M, Safari GH, Jaafari J. Effect of exposure to O_3, NO_2, and SO_2 on chronic obstructive pulmonary disease hospitalizations in Tabriz, Iran. Environmental Science and Pollution Research. 2015;22(4):2817-23.

[34] Medina-Ramon M, Zanobetti A, Schwartz J. The effect of ozone and PM10 on hospital admissions for pneumonia and chronic obstructive pulmonary

disease: a national multicity study. American journal of epidemiology. 2006;163(6):579-88.
[35] Anderson HR, Spix C, Medina S, Schouten JP, Castellsague J, Rossi G, *et al.* Air pollution and daily admissions for chronic obstructive pulmonary disease in 6 European cities: results from the APHEA project. Eur Respir J. 1997;10(5):1064-71.
[36] Ko FW, Hui DS, Lai CK. Worldwide burden of COPD in high- and low-income countries. Part III. Asia-Pacific studies. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2008;12(7):713-17.