UNIVERSITÀ DEGLI STUDI DI TORINO

QUANTIFICATION OF THE HEALTH EFFECTS OF EXPOSURE TO AIR POLLUTION (NO_2) IN TABRIZ, IRAN

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ABSTRACT:

Epidemiological studies show that long-term exposure to NO_2/NOx is associated with an increased risk of cancer. The mortality and morbidity rates due to NO_2 in the Tabriz city was determined considering the relative risk and baseline incidence provided by the World Health Organization (WHO) / European Center for Environment Health, Bilthoven Division using the $AirQ_{2.2.3}$ software to analyze the data. The results of this study showed that 0.85% (CI 95% 0.36 - 0.96) of acute myocardial infarction, 0.47% (CI 95% 0 - 0.94) of cardiovascular mortality and 9.28% (CI 95% 0.1 - 2.19) of hospital admissions for chronic obstructive pulmonary disease (COPD) can be attributed to NO_2 concentrations over 10 $\mu g/m^3$. According to this model, cases of cardiovascular deaths and acute myocardial infarction caused by NO_2 in Tabriz were about 0.23 and 0.10 percent of the total mortalities, respectively. In addition, about 0.9 percent of the total hospital admissions related to chronic obstructive pulmonary disease (HA COPD) was caused by NO_2. Therefore, due to this pollution, preventive measures and effective strategies for implementing policies related to reduce air pollution should be undertaken in Tabriz city.

KEYWORDS:

Quantification, Air pollution, NO_2, $AirQ_{2.2.3}$ software.

INTRODUCTION

Nitrogen dioxide (NO_2) is a gas with oxidant properties capable of contaminating ambient air in many urban and industrial contexts, as well as indoor air of homes with combustion appliances. NO_2 is mainly derived from oxidation of nitrogen oxide (NO) by atmospheric oxidants such as O_3. Regarding atmospheric pollution, released NO is rapidly oxidized by ozone and then converted to NO_2. The toxicity of $NO_2$is higher than that of NO [1]. New contaminants can be formed from photochemical reactions when organic aerosol and nitrate aerosols sulfate are used; they contributed significantly in PM_{10} and $PM_{2.5}$ aerosols and in their risk properties [2]. 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 appliances; but the main source of nitrogen dioxide in the urban area is the gas emitted by the public transports. NO_2 concentration varies from morning to night. The main sources of NO_2 in indoor environment are the natural gas cookers and the smoke produced by cigarettes. Acute short-term (one hour) effects and low concentrations have been observed in animals [3-5]. Observational data are derived from outdoors studies where NO_2 is one component among a complex mixture of different pollutants found in ambient air, and also from studies of NO_2 indoors exposure where its sources include unvented combustion appliances. Epidemiological studies over the past decade in Europe and worldwide showed increased mortality and illness associated with NO_2 exposure [6-9]; it was also estimated that 5% – 7% of lung cancers in non-smokers and ex-smokers could be attributed to exposure to high levels of air pollution, including NO_2, or vicinity to heavy-traffic roads [10]. Large meta-analyses of studies on the short-term health effects of NO_2 indicate a positive association between daily increases of NO_2 and natural, cardiovascular, and respiratory mortality [11, 12]. NO_2 could be a more relevant health-based exposure indicator than PM [13, 14]. Undesirable effects of NO_2 on the children health in urban areas with high concentrations of NO_2 have been identified [15-18]. An annual average for Air quality guideline values for NO_2 gas is 40 $\mu g/m^3$, which is lower than the toxicological threshold and represents a strong confirmation of the negative effects of outdoor NO_2.Owing to the continuous increase of health effects due to air pollution, European governments and the World Health Organization as well as other groups and associations, using the data collected during various studies have begun shaping method and environmental policy to assess the effects of air pollution on public health [19, 20]. Tabriz city is located in northwest of Iran in East Azerbaijan province between Eynali and Sahand mountains in a fertile area in shores of Aji River and Ghuri River. It has a semi-arid climate with regular seasons. With a population of over one and a half million peoples, it

is the fourth most populous city in Iran after Tehran, Mashhad and Isfahan. Tabriz is considered the second largest contaminated city after Tehran due to the presence of many large industrial plants and the high number of cars. Modern industries in this city include the manufacturing of machinery, vehicles, chemicals and petrochemical materials, refinery, cement, electrical and electronic equipment, home appliances, textiles and leather, nutrition and dairy factories and woodcraft [21]. Acute myocardial infarction is a common disease with serious consequences in mortality, morbidity, and cost to the society. Coronary atherosclerosis plays a pivotal part as the underlying substrate in many patients [22]. A link between ambient air pollution and cardiovascular disease, in particular myocardial infarction, has been suggested by a number of epidemiological studies and has attracted substantial attention within the cardiological community, as attested by the recent American Heart Association scientific statement on air pollution and cardiovascular disease [23]. There is convincing evidence of a relation between overall and cardiovascular mortality and the degree of air pollution on the previous day [24]. Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory airway disease that is described by hyper secretion, cough and inflammatory cell influx. COPD is a major cause of morbidity and mortality worldwide and continues to cause a heavy health and economic burden around the world, especially in the industrialized and the developing countries [25]. Air pollution has been certified as a trigger for exacerbation of COPD for more than fifty years and has lead to the expansion of air quality standards in many countries worldwide, leading to a substantial decrease of the level of variation of air pollutants derived from the burning of different fossil fuels [25]. The main objective of the present study was the assessment of health outcome due to NO_2 in Tabriz air.

MATERIALS AND METHODS

Study population and exposure assessment

This study was conducted during one year (from 21th Mars 2011 to 21th Mars 2012) in Tabriz city which has a population of 1 545 491 inhabitants. NO_2 concentration (in volumetric unit) in Tabriz was measured by the Eastern Azerbaijan Department of Environment (EADoE), using fix stations in six areas during 365 days in 2011. The six monitored stations were Abrasan (residential-commercial area in the eastern part of the city), Baqshomal (the downtown of the city), Health center (residential area in the northern part of the city), Hakim-nezami (residential area in the southern part of the city), Rah-ahan (Commercial Industrial area in the western part of the city) and Raste-kouche (commercial area in the downtown) (see Figure. 1). In Abrasan station the HORIBA model AP360 was used, while the Environ tech model M200 was used in

the other stations; these systems continuously monitored atmospheric NO_2 concentrations and involved a cross-flow modulated semi decompression chemiluminescence method. Raw data, such as daily average concentrations of NO_2, has been saved in a Microsoft Office Excel spread sheet and all processing mechanisms for conversion between volumetric and gravimetric units and etc, such as correction of temperature and pressure, coding, averaging and filtering were performed. Annual and seasonal average, maximum and annual 98th percentiles of NO_2 were obtained and concentrations were divided into 10 μg/m^3 categories. Then, the association between daily average concentrations of NO_2 and health impacts was estimated for one year by using AirQ$_{2.2.3}$ Software.

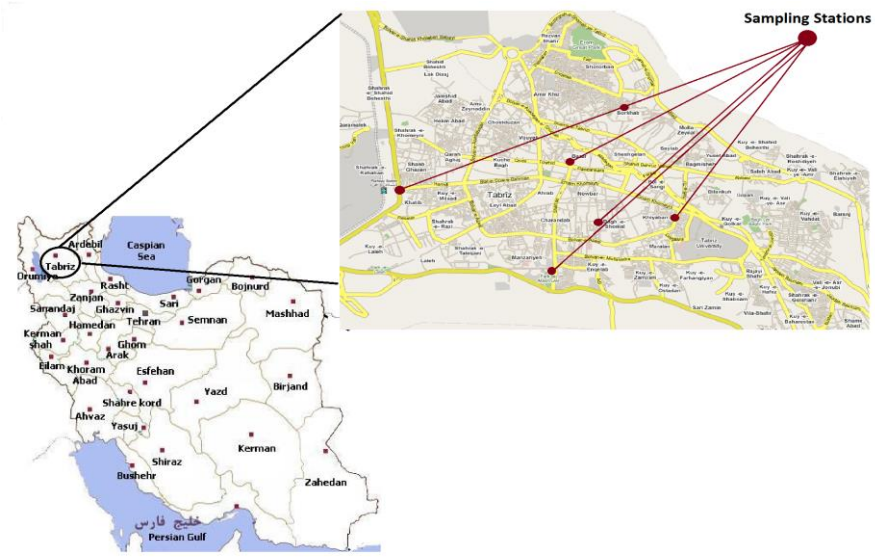

FIGURE.1 Map of the study area and locations of the monitored stations

Statistical analysis

The approach proposed by the World Health Organization (WHO) was applied using the AirQ$_{2.2.3}$ software developed by the WHO European Centre for Environment and Health, Bilthoven Division. This model is used to estimate the impacts of exposure to specific Air pollutants (confounders in any case) on the health of people living in a given period and area. This software consists of two quantification models and lifetime tables. Quantification model was used in this study, which was used to determine the Attributable Proportion (AP), the Relative Risk (RR) and the Based Incidence (BI) used for each health consequences. Relative risks (RR) with 95% confidence interval (CI) for each 10μg/m^3 increase in daily mean concentrations of NO_2 pollutants have been reported for hospital admissions due to chronic obstructive pulmonary disease (COPD) 1.0038 (1.0004 to 1.0094) by WHO. Also, baseline

incidences (BI), namely the incidence expected for a specific disease, per hundred thousand people have been presented: 132 for acute myocardial infarction (MI), 497 for cardiovascular disease and 101.4 for COPD by WHO. The assessment is based on the attributable proportion (AP), defined as the fraction of the health outcome in a given population attributable to exposure to a given atmospheric pollutant, assuming a proven causal relation between exposure and health outcome and no major confounding effects in that association. The AP can be easily calculated through the following general formula [26]:

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

Where AP is the attributable proportion of the health outcome, RR is the relative risk for a given health outcome, in category "c" of exposure, obtained from the exposure–response functions derived from epidemiological studies and P(c) is the proportion of the population in category "c" of exposure. If the baseline frequency of the health outcome in the population under investigation is known, the rate attributable to the exposure can be calculated as follows [26]:

$$IE = I \times AP \quad (2)$$

Where IE is the rate of the health outcome attributable to the exposure and I is the baseline frequency of the health outcome in the population under investigation. Finally, knowing the size of the population, the number of cases attributable to the exposure can be estimated as follows:

$$NE = IE \times N \quad (3)$$

Where NE is the number of cases attributed to the exposure and N is the size of the population investigated. RR gives the increase in the probability of the adverse effect associated with a given change in the exposure level, and comes from time-series studies where day-to-day changes in air pollutants over long periods are related to daily mortality, hospital admissions and other public health indicators. This program is used to estimate the impact of exposure to specific atmospheric pollutants on the health of people living in a given period and area. The assessment is based on the attributable proportion (AP), defined as the fraction of the health outcome in a given population attributable to exposure to a given atmospheric pollutant, assuming a proven causal relation between exposure and health outcome and no major confounding effects in that association.

Health End Point

Using the results of data processing and recorded data regarding the pollutants monitored in the considered stations of Tabriz the following information can be drawn:

In this studied city with the population equivalent to 1 545 491 people, the total cumulative of cardiovascular mortality due to NO_2 per hundred thousand can be calculated as follows:

$(M_{ct}/ P_t) \times 100000$ (4)

M_{ct}: The number of cardiovascular deaths from exposure to NO_2

P_t: Total Population

Unit: Number of deaths per 100000 persons

34.2 / 1 545 491 = 2.2 deaths per 100000 people

RESULTS AND DISCUSSION

In the table there are the days of exposure associated with the concentrations of NO_2 and the annual average of all stations (measured only in winter and in summer) and for the stations that have shown the highest and lowest concentrations. Accordingly, the average and maximum annuals of NO_2 in the considered stations of Tabriz were 33.54 and 78.52 $\mu g/m^3$ respectively. The maximum amount was related to Raste-khoche station located in the downtown and the minimum was related to Rah-ahan station that is in the western part of the city (Table.1).

TABLE 1. Highest and lowest concentrations of NO_2 ($\mu g/m^3$) corresponding to the stations for use in the AirQ2.2.3 model

Parameter	Raste-kouche (Maximum)	Rah-ahan (minimum)	Total stations
average annual	68.07	9.25	33.54
average summer	34.06	11.75	29.92
Average winter	38.3	8.52	24.82
98 percentiles annual	166.7	16.25	65.35
maximum annual	200.83	20.52	78.52
Maximum summer	200.83	20.1	78.52
Maximum winter	82.91	20.52	47.34

RR and estimated attributable proportions (AP) for acute myocardial infarction (MI) attributable to NO_2 are shown in table 2. According to the model default, the baseline incidence (BI) of this health endpoint for NO_2 was 132 per 100000 people; so, the number of excess cases was estimated for 16 persons at centerline of relative risk (RR=1.0036 and AP=0.8504). Moreover, the RR and estimated AP are presented in table 2 for cardiovascular mortality. BI obtained from model default was 497 per 100000 people for this health endpoint. Therefore, estimated number of excess cases were calculated to be 34 persons at centerline of relative risk (RR=1.002) and attributable proportions (AP=0.4742). Amounts of RR, AP and hospital admission chronic obstructive pulmonary disease (COPD) attributable to NO_2 using the model in moderate limits were estimated to be 1.0038, 0.8972, respectively. BI of this health endpoint was 101.4 per 100000, the estimated number of excess cases were 13 persons. Most of the resulting health consequences had been related to concentrations in the range of 20 to 60 $\mu g/m^3$ of pollutants (Table.2 and Figure.3). Table 2 represents the estimated Attributable proportion (AP) and number of excess cases in comparison to the cases giving a pollutant concentration of $10\mu g/m^3$. The numbers of excess cases regarding acute myocardial infarction, cardiovascular mortality and chronic obstructive pulmonary disease (COPD) are estimated based on the different Relative Risk (RR) and Attributable proportion (AP).

TABLE 2. Relative risk, Attributable proportion and number of persons suffering from type of health end point due to NO_2 exposure

Health End Point	Index Estimate	RR	Estimated AP (%)	Estimated number of excess cases (persons)
Acute myocardial infarction(BI=132 per 10^5 persons)	Lower	1.0015	0.3561	6.8
	central	1.0036	0.8504	16.3
	upper	1.0084	1.962	37.6
Cardiovascular mortality (BI=497 per 10^5 persons)	Lower	1	0	0
	central	1.002	0.4742	34.2
	upper	1.004	0.944	68
COPD (BI=101.4 per 10^5 persons)	Lower	1.0004	0.0952	1.4
	central	1.0038	0.8972	13.2
	upper	1.0094	2.1905	32.2

Figures 2-4 illustrates the NO_2 concentrations versus the cumulative of acute myocardial infarction, cardiovascular mortality and chronic obstructive pulmonary disease (COPD). The short-term health impacts of exposure to NO_2 above a reference value of 10 $\mu g/m^3$ are shown in these figures. Three ranges of relative risk were considered based on model default for assessing health effects of NO_2. Furthermore, baseline incidence (BI) values were also taken from model default. Charts drawing based on the cumulative number of each Health End Point showed number of cases in three modes, 5, 50 and 95 percent relative risks, leading therefore to three curves (related to lower, central and upper relative risks) in each graph, middle curve corresponds to a relative central risk, lower curve corresponds to a relative risk of 5% (underestimate) and the upper curve corresponds to a 95% relative risk (overestimate). We found about 0.9 percent of total hospital admissions related to the chronic obstructive pulmonary disease (HA COPD) was caused by NO_2. Moreover, the results of this study showed

that 0.85% (CI 95%; 0.36%; 0.96%) of acute myocardial infarction, 0.47% (CI 95%; 0; 0.94%) of cardiovascular mortality and 9.28% (CI 95%; 0.1%; 2.19%) of cardiovascular admissions for chronic obstructive pulmonary disease (COPD) can be attributed to NO_2 concentrations over 10 $\mu g/m^3$.

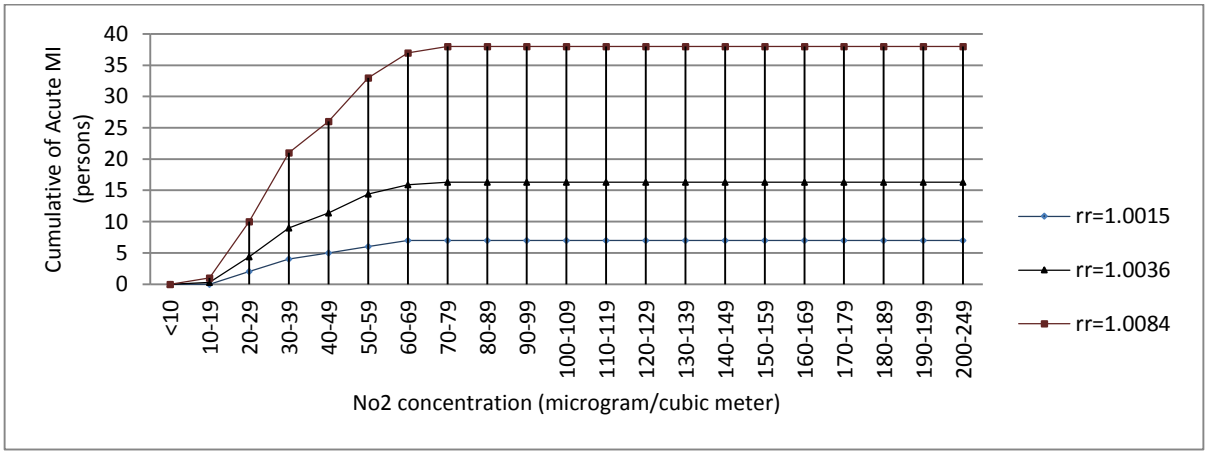

FIGURE.2 Relationship between Cumulative number of acute myocardial infarction (MI) and NO_2 concentration

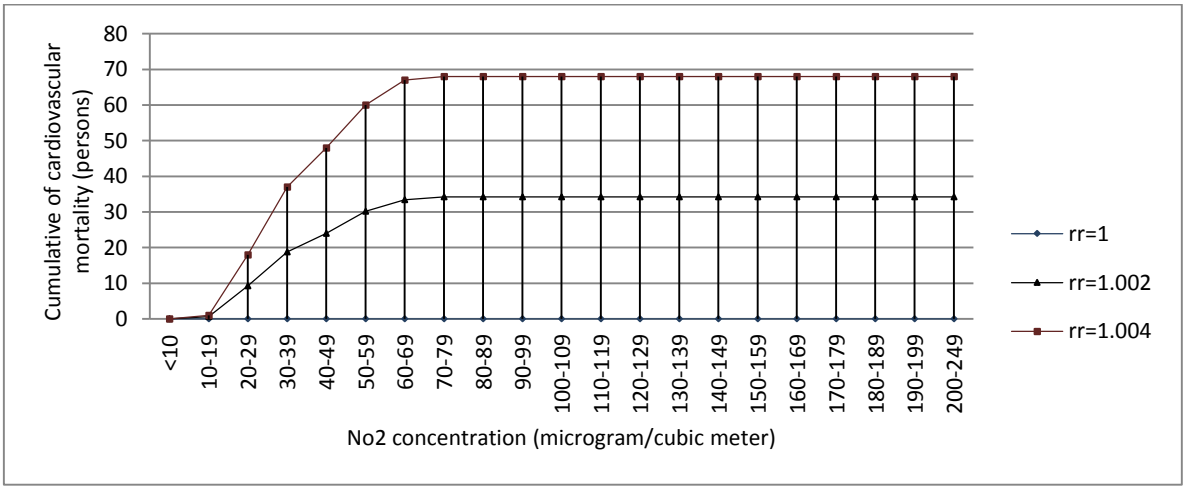

FIGURE.3 Relationship between Cumulative number of cardiovascular mortality and NO_2 concentration

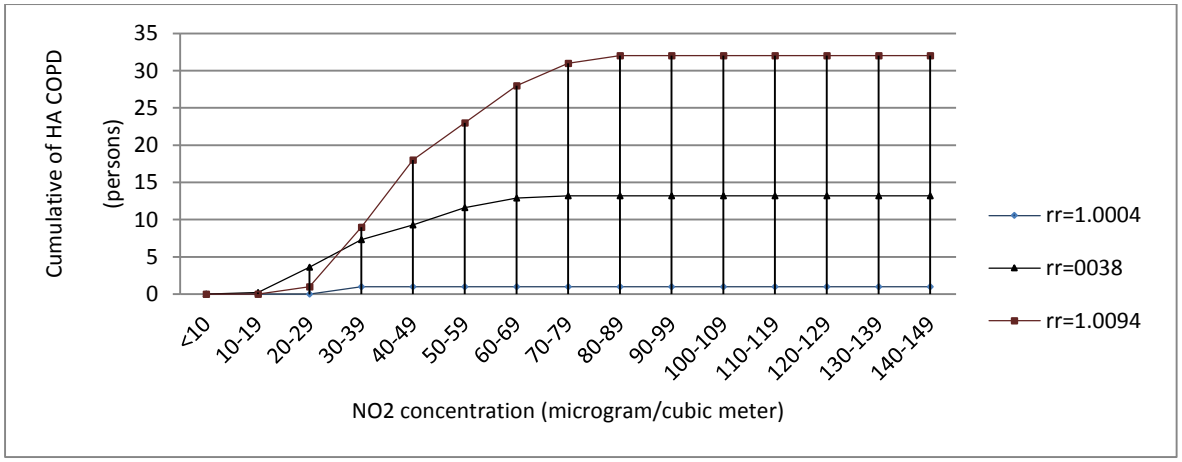

FIGURE.4 Relationship between Cumulative number of hospital admission for chronic obstructive pulmonary disease (COPD) and NO_2 concentration

Figures 2 to 4 illustrate the NO_2 concentration versus related to the health end point. Indicators of Relative Risk (RR) and Attributable Proportion (AP) for acute Myocardial Infarction (MI) to nitrogen dioxide defined on the Baseline Incidence (BI) were 132 from 10^5 persons according to the AirQ model from the WHO. The results showed three ranges of relative risks based on the model default, which were considered for assessing health effects of NO_2. Furthermore, baseline incidence (BI) values were also taken from the model default. For a population of one and half millions people and based on BI of 497 per one hundred thousand peoples each year, some 7 455 cardiovascular mortality cases can be expected annually; out of this number, 34 cases can be attributed to NO_2 concentrations above 20μg/m^3. Seventy percent of acute cardiovascular mortality cases occurred in days with pollution not exceeding 50 microgram per cubic meter, 97.7 percent of cardiovascular mortalities occurred in days with pollutant not exceeding 70 μg/m^3 and 87.9% of COPD cases occurred in days with pollutant not exceeding 60 μg/m^3. Although cardiovascular mortality had the lowest relative risk (RR) in centerline compared to acute cardiovascular mortality and chronic obstructive pulmonary disease, a high number of this health end point case was due to its higher BI value (497 per 10^5 peoples). On the other hand, a greater number of acute cardiovascular mortality cases compared to acute cardiovascular mortality (MI) ones were related to higher baseline incidence for MI. The comparison between acute cardiovascular mortality and obstructive pulmonary disease showed that the baseline incidence (BI) had more importance than relative risk (RR). This paper offers a study case using the WHO approach to assess the impact of atmospheric pollution on human health for people living in Tabriz, one of the most densely populated and industrialized areas in Iran, where the geographical features make the air quality among the

worst in the world. Considering short-term effects of NO_2 on the 1 500 000 inhabitants, causing an excess of acute myocardial infarction (MI) of 7 out of 38 people in a year. The NO_2 effect on cardiovascular mortality was an excess of about 68 cases in a year as well as the excess of hospital admissions for chronic obstructive pulmonary disease (COPD) of about 1 out of 32 people in a year. The number of excess cases was calculated for concentrations above 10 $\mu g/m^3$; so assuming a relatively low reference value, particularly compared to air standards. However, this was justifiable because the aim was to assess the human health impact of NO_2 as the air pollutant and not whether any particular air quality standards or guidelines were exceeded. As figures 2 to 4 show, health end point (number of outcomes) approximately under 70 $\mu g/m^3$of NO_2 has highly increased. This indicates that most days of exposure have been lower than of this concentration. In other words, the number of days of people exposure has been higher in this concentration interval. Gudarzi *et al*. exploited AirQ model to estimate the NO_2 hygienic effects in Tehran. Based on their results, almost 3.4% of all cases of the whole cardiovascular and respiratory mortalities are attributed to NO_2 concentrations, greater than 60 microgram per cubic meter [5]. The number of cases of myocardial infarction caused by exposure to NO_2 was reduced to zero when health outcome was closed to 5% range. In addition, if no appropriate measures to control air pollution and reduce health effects were taken, the corresponding RR was close to 95% range and the number of cases of myocardial infarction was estimated to be more than 2-fold increase in exposure to NO_2. This study has a number of limitations: one of the limitations of this approach is that the health impact focuses on individual compounds without considering the simultaneous exposure to several ones, which is what actually occurs. The health effects of atmospheric pollution are indeed the consequence of interactions between different air contaminants, and between these ones and other compounds of natural origin. Generally, in quantitative assessments of health effects, the interactions between different contaminants are not investigated as it would require a good knowledge of the mechanisms of toxicity for the different compounds, which is rarely available. A further limitation is due to the RR estimates derived in studies of different populations in comparison to that under investigation. Furthermore, this model does not consider intra-individual differences due to different behaviors inside the population considered (i.e active or passive smoking, mobility during the day, proximity to major roads, etc.). That's because the approach is ecological and not epidemiological. Finally, another limitation related to the exposure assessment is that the approach assumes that concentrations measured in specific sampling points are representative of the average exposure suffered from people living in Tabriz. Having said that, the following actions should be performed in order to reduce health effects caused by air pollution, so that

better quantification studies are recommended: 1- Restricting the use of underground resources and fossil material; measures are necessary to reduce the high urban traffic, which implies the raise of the level of urban public transport systems and correct traffic management, as well as the implementation of effective strategies to improve the quality of industrial productions. 2- The use of this model or other models is recommended to investigate and evaluate the effects of air pollution on health of people in other metropolitan country, and comparisons should be made. 3- Because the determination of the impact of air pollution on the related diseases and estimation of the health effects of air pollutants is a prerequisite, epidemiological indicators based on expert calculations are needed.

CONCLUSION

This study applied the AirQ software and the approach proposed by the WHO to provide quantitative data on the impact of NO_2 on the health of people living in a given area and this was the first attempt to assess health impacts of air pollution in Tabriz, Iran. Although the results of this study are in line with results of other researches around the world, despite the fact that the demographic, geographic and climate characteristics are different, there is still a high need to further studies to specify local RRs and BIs instead of WHO defaults. As mentioned above, air quality daily affects health conditions dramatically. Accordingly, cost-effective measures and management schemes should be considered to reduce air pollution concentrations and/or reduce exposure of people to air pollutants. The results are in line with those of other investigations and, despite the limitations, which are in common to similar studies, indicate that this method offers an effective and easy tool, helpful in decision-making.

REFERENCES

[1] Defense, H. (1996) Health effects of outdoor air pollution. American journal of respiratory and critical care medicine, pp.477-498.
[2] Traversi, D., Degan, R., De Marco, R., Gilli, G., Pignata, C., Ponzio, M., Rava, M., Sessarego, F., Villani, S. and Bono, R. (2008)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, pp.966-970.
[3] Al-Hurban, A. E. and Al-Ostad, A. N. (2010)Textural characteristics of dust fallout and potential effect on public health in Kuwait City and suburbs. Environmental Earth Sciences, pp.169-181.
[4] Fung, K., Krewski, D., Burnett, R. and Dominici, F. (2005) Testing the harvesting hypothesis by time-domain regression analysis. I: baseline analysis. Journal of Toxicology and Environmental Health, Part A, 68, pp.1137-1154.

[5] Goudarzi, G., Mohammadi, M. J., Angali, K. A., Neisi, A. K., Babaei, A. A., Mohammadi, B., Soleimani, Z. and Geravandi, S. (2011) Estimation of Health Effects Attributed to NO2 Exposure Using AirQ Model. Archives of Hygiene Sciences, pp.59-66.
[6] Gehring, U., Heinrich, J., Krämer, U., Grote, V., Hochadel, M., Sugiri, D., Kraft, M., Rauchfuss, K., Eberwein, H. G. and Wichmann, H.-E. (2006) Long-term exposure to ambient air pollution and cardiopulmonary mortality in women. Epidemiology, pp.545-551.
[7] Krzyzanowski, M. (2008) WHO air quality guidelines for Europe. Journal of Toxicology and Environmental Health, Part A, pp.47-50.
[8] Miri, A., Ahmadi, H., Ghanbari, A. and Moghaddamnia, A. (2007)Dust storms impacts on air pollution and public health under hot and dry climate. Int. J. Energy Environ, pp.101-105
[9] Samet, J. M., Zeger, S. L., Dominici, F., Curriero, F., Coursac, I., Dockery, D. W., Schwartz, J. and Zanobetti, A. (2000) The national morbidity, mortality, and air pollution study. Part II: morbidity and mortality from air pollution in the United States Res Rep Health Eff Inst, pp.75-79.
[10] Vineis, P., Hoek, G., Krzyzanowski, M., Vigna-Taglianti, F., Veglia, F., Airoldi, L., Overvad, K., Raaschou-Nielsen, O., Clavel-Chapelon, F. and Linseisen, J. (2007) Lung cancers attributable to environmental tobacco smoke and air pollution in non-smokers in different European countries: a prospective study. Environmental Health, pp.1-7.
[11] Touloumi, G., Katsouyanni, K., Zmirou, D., Schwartz, J., Spix, C., de Leon, A. P., Tobias, A., Quennel, P., Rabczenko, D. and Bacharova, L. (1997) Short-term effects of ambient oxidant exposure on mortality: a combined analysis within the APHEA project. American journal of epidemiology, pp.177-185.
[12] Stieb, D. M., Judek, S. and Burnett, R. T. (2003) Meta-analysis of time-series studies of air pollution and mortality: update in relation to the use of generalized additive models. Journal of the Air & Waste Management Association, pp.258-261.
[13] Kan, H. and Chen, B. (2003)A case-crossover analysis of air pollution and daily mortality in Shanghai. Journal of occupational health, pp.119-124.
[14] Schwartz, J., Dockery, D. W., Neas, L. M., Wypij, D., Ware, J. H., Spengler, J. D., Koutrakis, P., Speizer, F. E. and Ferris Jr, B. G. (1994) Acute effects of summer air pollution on respiratory symptom reporting in children. American journal of respiratory and critical care medicine, pp.1234-1242.
[15] Barnett, A. G., Williams, G. M., Schwartz, J., Best, T. L., Neller, A. H., Petroeschevsky, A. L. and Simpson, R. W. (2006) The effects of air pollution on hospitalizations for cardiovascular disease in elderly people in Australian and New Zealand cities. Environmental health perspectives, pp.1018-1023
[16] Sunyer, J., Basagana, X., Belmonte, J. and Anto, J. (2002) Effect of nitrogen dioxide and ozone on the risk of dying in patients with severe asthma. Thorax, pp.687-693.
[17] Seaton, A., Godden, D., MacNee, W. and Donaldson, K. (1995) Particulate air pollution and acute health effects. The Lancet, pp.176-178.
[18] Krzyzanowski, M., Kuna-Dibbert, B. and Schneider, J. (2005) Health effects of transport-related air pollution. WHO Regional Office Europe, pp.205.
[19] Krzyzanowski, M., Cohen, A. and Anderson, R. (2002) Quantification of health effects of exposure to air pollution. Occupational and environmental medicine, pp.791-793.
[20] KuÈnzli, N., Kaiser, R., Medina, S., Studnicka, M., Chanel, O., Filliger, P., Herry, M., Horak Jr, F., Puybonnieux-Texier, V. and Quenel, P. (2000) Public-health impact of outdoor and traffic-related air pollution: a European assessment. The Lancet, pp.795-801.
[21] Badescu, V. and Cathcart, R. (2011) Macro-engineering Seawater in Unique Environments: Arid Lowlands and Water Bodies Rehabilitation. Springer, pp. 323-329.
[22] Antman, E. M., Anbe, D. T., Armstrong, P. W., Bates, E. R., Green, L. A., Hand, M., Hochman, J. S., Krumholz, H. M., Kushner, F. G. and Lamas, G. A. (2004) ACC/AHA

guidelines for the management of patients with ST-elevation myocardial infarction—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). Journal of the American College of Cardiology, pp.671-719.
[23] Brook, R. D., Franklin, B., Cascio, W., Hong, Y., Howard, G., Lipsett, M., Luepker, R., (2004) Mittleman, M., Samet, J. and Smith, S. C. Air pollution and cardiovascular disease A statement for healthcare professionals from the expert panel on population and prevention science of the American Heart Association. Circulation, pp.2655-2671.
[24] Sarnat, J. A., Schwartz, J. and Suh, H. (2001) Fine particulate air pollution and mortality in 20 US cities. N Engl J Med, pp.1253-1254.
[25] Ghozikali, M. G., Mosaferi, M., Safari, G. H. and Jaafari, J. (2014) Effect of exposure to O3, NO2, and SO2 on chronic obstructive pulmonary disease hospitalizations in Tabriz, Iran. Environmental Science and Pollution Research, pp.1-7.
[26] Fattore, E., Paiano, V., Borgini, A., Tittarelli, A., Bertoldi, M., Crosignani, P. and Fanelli, R. (2011) Human health risk in relation to air quality in two municipalities in an industrialized area of Northern Italy. Environmental research, pp.1321-1327.