



# Impact of exposure to ambient air pollutants on the admission rate of hospitals for asthma disease in Shiraz, southern Iran

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## H I G H L I G H T S

- Asthma hospital admissions due to NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> were estimated for Shiraz, Iran.
- AirQ<sub>2.2.3</sub> software was used for developing predictive models.
- Attributed equivalent modeled for hospital admission due to asthma disease (HAAD).
- The number of extra cases of HAAD for <15 years was estimated to be 273 for 2016.
- The yearly average concentration of SO<sub>2</sub> was 8.62 times more than the WHO guideline.

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## A B S T R A C T

Asthma is a common chronic respiratory disease in the world. Short-term exposure to ambient air pollutants is closely related to acute respiratory diseases and asthmatic symptoms. The purpose of this research was to estimate the correlation between exposure to three air pollutants (O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub>) and hospital admission because of asthmatic disease (HAAD) in the city of Shiraz, southern Iran. The data were collected from the two real-time monitoring stations located in this city. The acquired information was used for developing predictive models by the AirQ software. The findings of this study were reported for two age groups (<15 and 15–64 years old). The highest levels of O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> were obtained 187.33 µg/m<sup>3</sup>, 34.1 µg/m<sup>3</sup>, and 491.2 µg/m<sup>3</sup> in 2016, respectively, and 227.75 µg/m<sup>3</sup>, 92.26 µg/m<sup>3</sup>, and 190.21 µg/m<sup>3</sup>, respectively, in 2017. Among the mentioned pollutants, the yearly average concentration of SO<sub>2</sub> was 8.62 times more than the WHO guideline, during the studied times. The number of extra cases of HAAD for <15 years and 15–64 years caused by the air pollutants in Shiraz were estimated to be 273 and 36, respectively, in 2016, and 243 and 30 for 2017, respectively. The results of this work displayed that air pollutants have caused respiratory problems in Shiraz city. The AirQ model is a facile and potential tool for the prediction of asthma disease to reduce the health risk of atmospheric pollutants in the worldwide.

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## 1. Introduction

Asthma is one of the most common respiratory diseases, affecting 5 to 18 percent of people worldwide, especially children. People suffering from this disease have symptoms such as breathlessness and wheezing, which differ in frequency and severity from person to person (To et al., 2013). In involved people, asthma

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symptoms usually occur several times a day or week. For some people, these symptoms get worse during physical activity or at night. During an asthma attack, the lining of the bronchial tubes inflates, and therefore, with narrowing airways, the flow of air into and out of the lungs decreases. Asthma is often accompanied by symptoms such as sleeplessness, daytime fatigue, reduced activity levels, and school and work absenteeism. This type of disease has a relatively low mortality rate compared to other chronic diseases (Ghaffari et al., 2017).

Trasande and Thurston (2005) reported that acute respiratory syndromes embodied particularly in children with asthma were related to the ambient air pollutants such as particulate matters (PM<sub>2.5,10</sub>), ozone (O<sub>3</sub>), and nitrogen dioxide (NO<sub>2</sub>). Moreover, last studies express a continuously increasing trend in outpatient visits and hospitalizations due to asthma incidence, likely resulting from exposure to the ambient air pollutants (Riedl and Diaz-Sanchez, 2005). The sources of air pollutants may create asthma, for example, the combustion of fossil fuels can cause airway inflammation via the mechanisms of oxidative stress (Poole et al., 2019). The organic and nonorganic pollutants at high concentrations, especially those placed on ultrafine particles (<0.1 μm), cause to intensify asthma symptoms and to reduce lung function (Ghaffari et al., 2017). Asthma is more likely to occur in the homes and schools located in high-traffic areas than in low-traffic areas (Hauptman et al., 2020). However, in Iran like the rest of the world, mobile and stationary sources, including motor vehicles, industries, home heating, emit a wide variety of outdoor airborne pollutants (Seifi et al., 2019). Concerning the incidence of air pollution events following extreme dust storms, it can be declared that natural phenomena have an important role in the creation of asthma (Khaniabadi et al., 2017). In a study reported that exposure to aeroallergens such as pollen major trigger of asthma exacerbations (Murray et al., 2006). Nitrogen dioxide (NO<sub>2</sub>) and sulfur dioxide (SO<sub>2</sub>) are classified as primary criteria air pollutants while ozone (O<sub>3</sub>) is classified as the secondary one. Nitrogen dioxide (NO<sub>2</sub>) is one of a group of highly reactive gases that produce thought oxidation processes in which emitted nitrogen oxide reacts with atmospheric oxidizers such as O<sub>3</sub>. Road vehicles, heaters, and industrial activities with the burning of organic fuels can emit high-level NO<sub>2</sub> in the atmosphere. Sulfur dioxide (SO<sub>2</sub>), regarded as a highly reactive corrosive gas in atmospheric pollutants, is mainly released from fossil fuel combustion in mining and industrial facilities. Both NO<sub>2</sub> and SO<sub>2</sub> pollutants are related to adverse impacts on the respiratory health (Ghaffari et al., 2017).

The AirQ software, designed by the WHO European Center for Environment and Health, is a valid and reliable instrument to assess the potential health impacts of air pollution and enable evaluation of scenarios specified by varied pollutants (Conti et al., 2017). This software collects, manages, and displays data obtained from criteria air pollutants (Conti et al., 2017). The mortality and morbidity due to exposure to outdoor air pollution in Mashhad metropolis have been estimated using the AirQ software (Miri et al., 2016). Asl et al. (2018) have quantified the health impacts of ambient air pollutants using the AirQ model approach in Hamadan city. Similar researches have used this software to estimate the health effect of air pollutants in other cities (Mokhtari et al., 2015; Nikoonahad et al., 2017). Based on Pierangeli et al. (2020) study, the number of asthma cases attributable to NO<sub>2</sub> and PM<sub>2.5</sub> (percentage of total cases) in Barcelona estimated to be 454 (18%) and 478 (19%), respectively. The relationship between short-term exposure to air pollutants (PM<sub>2.5</sub>, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub>) and the increase of asthma exacerbations among children has been revealed (Liu et al., 2020).

This investigation was aimed to estimate asthma disease as a cause of admission to hospitals due to exposure to O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> contaminants in Shiraz, Iran. Shiraz is the biggest city located in southern Iran with a semi-arid climate, so the acquired findings of this work can have broad applications for other cities in the world with a similar climate.

## 2. Methodology

### 2.1. The study area

Shiraz with a citizen count of ~1.86 million (49.57% woman and 50.43% man) is the central city of Fars Province and situated in southern Iran (Bonyadi et al., 2020). This city with a warm and semi-arid climate, an average annual temperature of 18.6 °C, average wind speed of 10.78 km/h, average annual humidity of 39.5%, and an average annual rainfall of 274.8 mm is located in geographical coordination of 29°36' N and 52°32' E and the elevation of 1540 m (Gharehchahi et al., 2013).

### 2.2. The software of AirQ<sub>2,2,3</sub>

In this research, the AirQ model in different scenarios was used for measuring health outcomes resulting from short-term exposure to specific air pollutants including O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub>. AirQ<sub>2,2,3</sub> is a valid and reliable software for assessing the potential health effects of oxidant air pollutants, which combines the information of exposure-response and, then, estimates the health effects in a given population.

A causal association was presumed between the risk factor and the health impact to promote the validity of calculates in this program. In a specific time and city, the assessment of the health consequences of exposure to certain air contaminants was performed using the international software of AirQ<sub>2,2,3</sub>.

The hygienic and epidemiological assessment was performed based on the attributable equivalent (AE), defined as the portion of the health outcomes in the desired population attributable by exposure to given atmospheric air pollutants, presuming a confirmed vital relationship between exposure and health consequence and no influenced by a notable interferences in that association (Bonyadi et al., 2020). The attributable equivalent (AE), which has a link to the exposure of an exact people during a fixed time, is calculated by the following formula:

$$AE = \frac{\sum([RHR(c)-1] \times P(c))}{\sum(RHR(c) \times P(c))} \quad (1)$$

Where RHR(c) denotes the relative health risk due to an investigated pollutant in the aimed group, and P(c) denoted the equivalent exposed case in category "c".

The RHR parameter revealing the amount of a specified contaminant's effect on the health by an alteration in exposure to the polluted air is acquired via studied periods that assess the concentration alterations of air contaminants and their impacts on long-term health series (Rovira et al., 2020). This work was done based on the default WHO data available through AirQ software. The RHR values for O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> were obtained from similar works (Ghaffari et al., 2017).

After specification the main frequency of health effects in the studied population, then the attributable exposure rate (AER) of the health effect can measure as:

$$\text{AER} = I \times \text{AE} \quad (2)$$

where the 'I' factor shows the baseline frequency of the health effect in the studied population. In this study, the proposed baseline frequency by WHO were used.

Finally, by Eq. (3) and knowing the size of the Shiraz population (N), the number of cases attributed to the exposure (NE) is estimated as follows:

$$\text{NE} = \text{AER} \times N \quad (3)$$

As no time-series survey has yet been conducted in Iran, therefore, the default data provided by WHO for the AirQ software were used. In the APHEA project, RHR amounts for NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> were obtained from previous studies (Touloumi et al., 1996).

### 2.3. Data collection

In the current research, the information for air pollutants of O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> was supplied by the Fars's Institute of Environment. Two fixed monitors of criteria air pollution in the Shiraz city (Caserone gate and Setad stations) were used which cover the data from January 2015 to January 2017. The model of the devices in both stations was Environ-Tech. The devices are checked, adjusted, and calibrated according to the program of the Iranian Department of Environment. The map of fixed-air monitoring stations in the Shiraz city is illustrated in Fig. 1.

The air pollution data were entered into Microsoft Excel format. Therefore, the information was transformed into the required format for the AirQ software. Before evaluation, data must be analyzed based on criteria listed by WHO including, the ratio of the number of valid data for the summer season to the winter data and vice versa should not be more than 2 and to achieve an hourly average of data, at least 75% of the data must be valid.

The assessment of the adverse health effects using the AirQ software is associated with the level and type of inhaled pollutants. Thus, information units were modified to the weight-volume unit (g/μm<sup>3</sup>) based on temperature and pressure conditions for the gaseous contaminants and then categorized at the intervals of 10 μg/m<sup>3</sup>. For all oxidative air contaminants, maximum annual, average seasonal, and 98th percentiles were calculated. The data were also represented as "daily".

## 3. Result and discussion

### 3.1. The level of air pollutants in the Shiraz atmosphere

The statistical findings of the oxidant pollutants survived in this study have been showing in Table 1. From findings, the highest annual levels for O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> were obtained 187.33, 34.1, and 491.2 μg/m<sup>3</sup> in 2016, respectively, and whereas for 2017 the maximum level for these pollutants was found to be 227.75, 92.26, and 190.21 μg/m<sup>3</sup>, respectively, in 2017. Among the pollutants mentioned above, the yearly average concentration of SO<sub>2</sub> was 8.62 times more than the WHO guideline, during study times (World Health Organization, 2006). A possible reason for this issue is the low quality of fuel in Iran.

Considering the results listed in Table 1, the concentrations of O<sub>3</sub> and SO<sub>2</sub> in summer were higher than in winter. This can be interpreted by the enhance in photochemical activity with high temperature due to the increase in the intensity of solar radiation, the intensity of dust storms, the lack of adequate rainfall, and low wind speed in this session (Asl et al., 2018). Based on the research of Fattore et al. (2011), the maximum NO<sub>2</sub> concentration, 76 mg/m<sup>3</sup> was detected in winter, while the maximum concentration of O<sub>3</sub> (174 mg/m<sup>3</sup>) was obtained in summer. Significant negative correlations were stated between the atmospheric pollutants and atmospheric conditions (wind speed and relative humidity) (Asl et al., 2018).

From Table 1, the level of pollutants in summer has enhanced significantly compared to winter (P-value <0.05), which can be attributed to increased adverse atmospheric conditions and high traffic in Shiraz city, which this is due to the tourist arrival in the city and also sulfur content in the fuel of vehicles (Gharehchahi et al., 2013; Chu Van et al., 2018). The results of this study are consistent with other studies (Ooka et al., 2011; Kalabokas et al., 2013).

### 3.2. Hospital admission due to asthmatic disease based on the AirQ software

In this study, health outcomes resulting from short-term exposure to oxidant pollutants including O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub>, were measured by using the AirQ model in different scenarios. Table 2 shows incidence, RHR, AE, and the number of extra cases in a year due to short-term exposure above 10 μg/m<sup>3</sup> for O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub>. Based on the results depicted in Table 2, the maximum attributable equivalent (AE) for HAAD < 15 years old was related to SO<sub>2</sub> with 14.44% and 18.18%, respectively, in both 2016 and 2017.

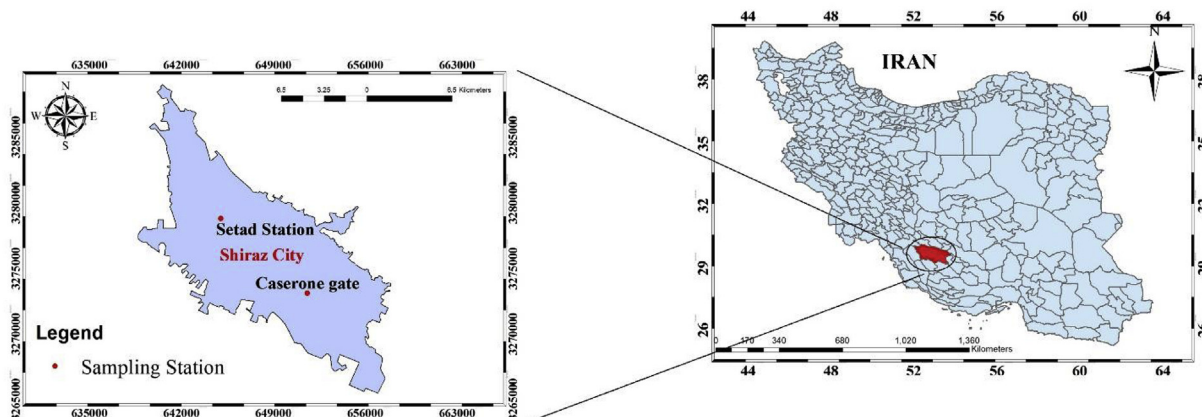


Fig. 1. The investigated area and air monitoring sites (Shiraz, Iran).

**Table 1**  
Summary of the concentrations of studied air pollutants ( $\mu\text{g}/\text{m}^3$ ) in Shiraz city during 2015–2017.

| Parameter |                       | O <sub>3</sub> |           | NO <sub>2</sub> |           | SO <sub>2</sub> |           |
|-----------|-----------------------|----------------|-----------|-----------------|-----------|-----------------|-----------|
|           |                       | 2015–2016      | 2016–2017 | 2015–2016       | 2016–2017 | 2015–2016       | 2016–2017 |
| Average   | Annual                | 46.16          | 45.31     | 14.35           | 16.45     | 120.05          | 52.58     |
|           | Summer                | 36.48          | 43.83     | 17.95           | 5.59      | 95.85           | 70.06     |
|           | Winter                | 72.04          | 45.81     | 10.43           | 28.18     | 149.61          | 39.58     |
|           | 98 percentiles annual | 155.34         | 155.93    | 31.14           | 92.12     | 437.19          | 177.19    |
| Maximum   | Annual                | 187.33         | 227.75    | 34.1            | 92.26     | 491.23          | 190.21    |
|           | Summer                | 108.76         | 227.75    | 34.1            | 6.58      | 491.23          | 190.21    |
|           | Winter                | 99.07          | 15814     | 19.72           | 92.26     | 404.51          | 133.59    |
|           |                       |                |           |                 |           |                 |           |

While, the highest AE for HAAD >15–64 years was attributed to O<sub>3</sub> with 2.71% and 2.36%, respectively, in 2016 and 2017. From Table 2, the number of extra cases for HAAD <15 and HAAD >15–64 caused by oxidant air pollutants in Shiraz was estimated to be 273 and 36 cases, respectively, in 2016, and the values for equivalent pollutants during the year 2017 were observed as 243 and 30 cases. Fig. 2 indicates the relationship between oxidant pollutant concentrations and the cumulative number of HAAD <15 years and HAAD >15–64 years in central RHR from 2016 to 2017. As shown in Fig. 2, the number of excess cases for HAAD <15 related to SO<sub>2</sub> is higher than those of other oxidant pollutants in both 2016 and 2017. Also, findings showed that the impact of this pollutant on the age group less than 15 years old is more severe than that of the age group of 15–64 years old. This finding may be due to the high sensitivity of children/teenagers with inflammatory markers to oxidative stress correlated to atmospheric pollution and, therefore, the asthma risk is greater for this age group (Delfino et al., 2014). These findings demonstrate the irrefutable portion of air contaminants on the overall mortality cases produced by respiratory diseases (Karimi et al., 2019; Phosri et al., 2019). On the other hand, some researchers proposed the adverse health effects of pollutants at fewer levels than the recommended values of atmospheric pollutant guidelines (like WHO or USEPA guidelines), which reveals the weakness of standards to conserve people's health.

In a systematic review performed by Clark et al. (2010), NO<sub>2</sub> was introduced as the most important pollutant causing asthma. They also expressed that SO<sub>2</sub> in industrial areas was related to asthma risk. Many other types of research have also shown that traffic-related air pollution causes a probability of asthma disease (Brauer et al., 2007; Morgenstern et al., 2008; Mortimer et al., 2008; Strickland et al., 2010). The NO<sub>2</sub> gas acts as a basic proxy for traffic-

related air pollution (TRAP) and is the main part of urban air pollution, primarily caused by the combustion of fossil fuels, and yet, traffic and road pollution were correlated with up to 80% of atmospheric NO<sub>2</sub> in cities. The involvement of exposure to NO<sub>2</sub> in pediatric asthma is due largely to the activation of innate immune responses (Liu et al., 2020).

According to the findings of Fig. 2, the number of extra cases for HAAD >15–64 years was mainly attributed to O<sub>3</sub> in both 2016 and 2017. The cumulative number of hospitalizations was increased in a concentration of more than 30 ppb O<sub>3</sub>. The sources of O<sub>3</sub> include the VOCs and CO emissions from industries, high traffic districts, as well as incomplete combustion in residential areas. The photochemical reaction between nitrogen oxides, volatile organic compounds, heat, and sunlight is the predominant mechanism to produce atmospheric O<sub>3</sub> (Goudarzi et al., 2015; Asl et al., 2018). The impact of exposure to O<sub>3</sub> on pediatric asthma is complex, as O<sub>3</sub> can function in two opposite ways, in that O<sub>3</sub> has both inflammatory and antiviral effects. Ozone via the production of oxygen radicals increases oxidative stress, inflammation, and epithelial cell damage, which may cause asthma exacerbation, whereas O<sub>3</sub> has also been observed to be protective from some respiratory viral infections, which is an initial precipitating factor for pediatric asthma (Liu et al., 2020). Based on the effect of air pollutants in warm weather on Australian children in a specific period, it has been expressed that ozone has the greatest a five-day cumulative effect and enhanced 11.7% (95% CI 5.8–17.9%) the HAAD risk for children per 10 ppb increase in the ozone level (Chen et al., 2016). Gryparis et al. (2004) in the study on 23 cities/areas throughout Europe have been stated that an increase in the O<sub>3</sub> level by 10  $\mu\text{g}/\text{m}^3$  is associated with 1.13% (95% CI, 0.62–1.48) in the number of the deaths due to respiratory diseases.

**Table 2**  
Attributable equivalent (AE) expressed as percentage and number of extra cases in a year due to short-term exposure above 10  $\mu\text{g}/\text{m}^3$  for SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub> (Chaffari et al., 2017).

| Health endpoint                         | Incidence <sup>a</sup> | RHR (95% CI <sup>b</sup> ) per 10 $\mu\text{g}/\text{m}^3$ | Pollutant       | Estimated AE (%) <sup>c</sup> |                     | Extra cases (uncertainty range) <sup>c</sup> |                    |
|---|------------------------|--|-----------------|-------------------------------|---------------------|--|--------------------|
|   |                        |  |                 | 2015–2016                     | 2016–2017           | 2015–2016                                    | 2016–2017          |
| Hospital admissions asthma <15 years    | 100                    | 1.0012 (1–1.0074) <sup>d</sup>                             | O <sub>3</sub>  | 0.00 (0.00–2.94)              | 0.00 (0.00–2.55)    | 0.0 (0.0–54.8)                               | 0.0 (0.0–47.6)     |
|   | 100                    | 1.0052 (1.0012–1.0098) <sup>e</sup>                        | NO <sub>2</sub> | 0.273 (0.063–0.514)           | 0.064 (0.014–0.121) | 5.1 (1.2–9.6)                                | 1.2 (0.3–2.3)      |
|   | 100                    | 1.015 (1.0052–1.025) <sup>e</sup>                          | SO <sub>2</sub> | 14.44 (5.53–21.96)            | 13.02 (4.93–19.97)  | 268.8 (102.9–408.6)                          | 242.3 (91.8–371.6) |
| Hospital admissions asthma >15–64 years | 66                     | 1.003 (1–1.0156)   | O <sub>3</sub>  | 2.71 (0.00–10.31)             | 2.36 (0.00–9.05)    | 33.4 (0.0–126.6)                             | 29 (0.0–111.1)     |
|   | 66                     | 1.0058 (1.0006–1.011)                                      | NO <sub>2</sub> | 0.305 (0.031–0.577)           | 0.071 (0.007–0.135) | 3.7 (0.4–7.1)                                | 1 (0.1–1.7)        |
|   | 66                     | 1 (1–1.0068)   | SO <sub>2</sub> | 0.00 (0.00–7.11)              | 0.00 (0.00–6.36)    | 0.00 (0.00–87.3)                             | 0.0 (0.0–78.1)     |

<sup>a</sup> Crude rate per 100,000 inhabitants.

<sup>b</sup> CI: Confidence intervals.

<sup>c</sup> Obtained using the lower and upper RHR values.

<sup>d</sup> 1 h average.

<sup>e</sup> Daily average.

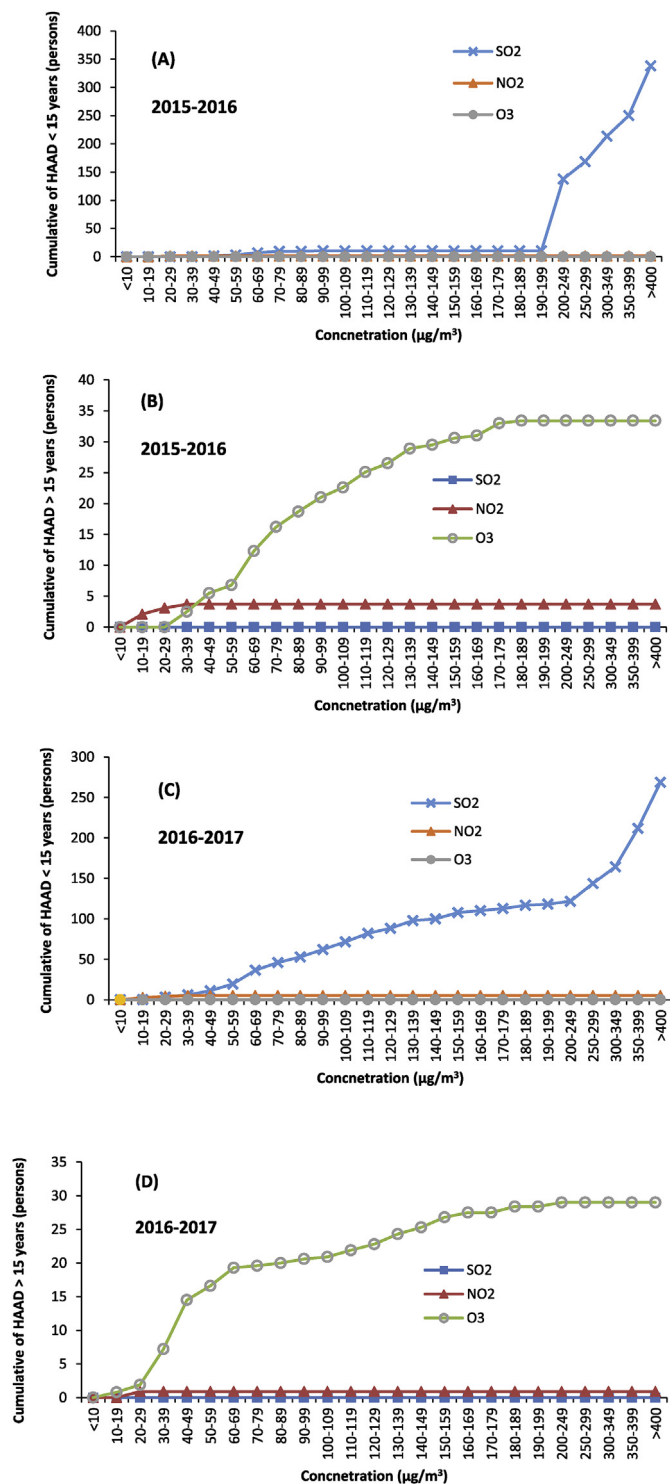


Fig. 2. Relationship between pollutants concentration and cumulative number of HAAD (A) < 15 years old during 2015–2016, (B) > 15 years old during 2015–2016, (C) < 15 years old during 2016–2017, and (D) > 15 years old during 2016–2017.

### 3.3. Limitations of this research

Although the use of AirQ software is developed and recommended by the World Health Organization, it has some shortcomings.

This software considers the effects of each pollutant separately, while the toxicity of the pollutant in the atmosphere may change under conditions of light and volatile organic matter (Naclerio et al.,

2020). Therefore, this software is unaware of the cumulative effects of atmospheric pollutants on humans. However, there are several reports that climatic conditions, global warming, and new factors could affect the health effects of pollutants in the atmosphere (D'Amato et al., 2015; Kajino et al., 2017).

The RHR factor is based on reports from American and European countries that have different demographic characteristics, and its generalization to developing countries could take the results far from reality. Therefore, the researchers of each country should obtain and apply this factor based on the field data.

A further limitation is that the approach assumes that the concentration of pollutants measured in specific sampling points is representative of the average exposure of people living in Shiraz city with an area of ~240 km<sup>2</sup>. One solution is to use mobile stations.

The software assumes that all people are equally exposed to pollutants and exposed to them all the time, although we know this is not the case.

Despite the shortcomings, the World Health Organization (WHO) has proposed to use this tool for calculating the health effect of criteria air pollutants and various well-known editors around the world have accepted the application of AirQ software (Asl et al., 2018; Bonyadi et al., 2020; Luo et al., 2020; Rovira et al., 2020).

## 4. Conclusions

The overall goal of this study was to calculate the relationship between hospital admissions due to asthma and airborne pollutants (NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub>) during the years 2015–2017. Based on findings, Shiraz city had the maximum concentration of pollutants in the years 2016 and 2017 was corresponded to SO<sub>2</sub> and O<sub>3</sub>, respectively. The yearly average concentration of SO<sub>2</sub> was 8.62 times more than the WHO guideline, during study times. Accordingly, this pollutant had the maximum adverse effect on Shiraz citizenships' health. In the study area for both 2016 and 2017, the highest number of extra cases were linked to SO<sub>2</sub> and O<sub>3</sub> with the most effect on HAAD <15 and HAAD >15 years, respectively. This research suggests to local and regional policymakers that management programs like public transportation development and fossil fuel substitution need to be implemented to reduce the air pollutants concentration as much as possible. Finally, although some studies have used this model to estimate health impacts due to exposure to air pollution, we also suggest this model for the evaluation of HAAD.

### Authorship Contribution Statement

Ziaeddin Bonyadi: Software, Writing - original draft. Hossein Arfaeinia: Methodology, Conceptualization, Moradali Fouladvand: Conceptualization and review. Sima Farjadfar: Methodology. Mohsen Omidvar: Methodology, Validation. Bahman Ramavandi: Supervision, review& editing.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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