DISTRIBUTION AND NUMBER OF ISCHEMIC HEART DISEASE (IHD) AND STROKE DEATHS DUE TO CHRONIC EXPOSURE TO PM$_{2.5}$ IN 10 CITIES OF IRAN (2013 - 2015); AN AIRQ+ MODELLING

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ABSTRACT:

**Introductions:** Particulate air pollution is known as a major risk factor of ischemic heart disease (IHD) and stroke. The aim of this study was to estimate the premature IHD and stroke deaths attributed to long-term exposure to PM$_{2.5}$ in 10 cities of Iran during March 2013 to March 2015 using AirQ+ model.

**Materials and methods:** Ten cities of Iran including Tehran, Mashhad, Isfahan, Shiraz, Tabriz, Ahvaz, Arak, Sanandaj, Khoram Abad, and Ilam were chosen, and their air quality data were acquired from Department of Environment (DoE) and Tehran Air Quality Control Company (AQCC). Validation of monitoring stations were accomplished according to WHO and APHEKOM criteria for health impact assessment of air pollution. The number of deaths due to IHD and stroke was estimated using AirQ+, which is developed by WHO.

**Results:** The total number of IHD and stroke deaths in the March 2013-March 2014 and March 2014-March 2015 periods were 15479 and 15321 deaths, respectively. In case of both IHD and stroke mortality, the highest number of IHD and stroke deaths was estimated to be in Tehran, Mashhad and Isfahan, respectively. The highest number of attributable deaths per 100,000 population were estimated to be in Ahvaz and Isfahan. The average of excess IHD and stroke deaths due to exposure to PM$_{2.5}$ in all cities were 84 and 41 per 100,000 population, respectively.

**Conclusions:** The results of this study indicated the necessity of urgent actions to improve the outdoor air quality in Iranian cities.

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be the result of exposure to ambient air pollution [2]. Epidemiological studies have shown positive associations between air pollutants such as particulate matter of aerodynamic diameter less than 10 μm (PM$_{10}$) and 2.5 μm (PM$_{2.5}$), nitrogen dioxide (NO$_2$), sulphur dioxide (SO$_2$), ozone (O$_3$) and carbon monoxide (CO) and adverse health outcomes [3-6]. Particulate air pollution was introduced by International Agency for Research on Cancer (IARC) as carcinogen to human [7]. Coronary heart disease (CHD) or ischemic heart disease (IHD) is the most common cardiovascular disease [8]. Many studies have been conducted the relationship between long-term exposure to particulate air pollution and cardiovascular mortality [9]. In a cohort study, cardiovascular mortality increased by 8-18% per 10 μg/m$^3$ increase of PM$_{2.5}$ concentrations; however, a weak association was found between similar amount of PM$_{1.5}$ and respiratory mortality [10]. In another cohort study, the most significant association was found between PM$_{2.5}$ in one side, and IHD, cardiovascular diseases, and lung cancer in the other side [11]. Despite the counties in Europe and Northern America, Middle Eastern countries are experiencing high concentrations of airborne particulates, and incidence of cardiovascular diseases. Many studies have been conducted to evaluate the relationship between air pollution and cardiovascular diseases, particularly IHD [12-14]. Airborne concentrations of particulate matter are associated with high blood pressure and plasma viscosity. These factors are indicators of hemodynamic disorders and elevated amount of inflammation in circulatory system [15, 16]. These are known as major risk factors for stroke [17]. In a study on the effect of acute exposure to low levels of different fractions of particulates on stroke incidence in Finland, a significant relationship was found between particulates and incidence of stroke in warm seasons [18]. In general, less studies have been carried out about the association between air pollution and stroke, rather than other health outcomes. Some of these studies have been performed in Asia, where high concentrations of particulate air pollution presents. Health impact assessment of air pollution can be useful for health authorities and policy-makers. Different methods and tools have been developed for this purpose, such as AirQ, BenMap, AirQ+, etc. AirQ+ is a software tool for quantifying the health impacts of air pollution developed by the WHO Regional Office for Europe. The software can handle different air pollutants such as PM$_{2.5}$, PM$_{10}$, NO$_2$, O$_3$, and black carbon (BC). This software has been developed to assess the effects of long-term and short-term exposure to ambient air pollution. In addition, AirQ+ can estimate the effects of household air pollution related to Solid Fuel Use (SFU). Acute and chronic mortality and morbidity of several health outcomes can be considered to enter the model. The underlying scientific evidence on health effects from ambient air pollution used in the software is derived mainly from epidemiological studies conducted in Western Europe and North America [19]. Iran is facing serious problems in case of ambient air pollution [20]. Several health impact assessments have been carried out in Iran to estimate the health effects of air pollution [21-24]. In a study which AirQ 2.2.3 was used to estimate the health effects of PM$_{10}$, PM$_{2.5}$, O$_3$, NO$_2$, and SO$_2$ during 2013-2016 period [24]. In another study, gender-specific lung cancer deaths due to exposure to PM$_{2.5}$ were estimated by AirQ+ for 10 cities of Iran during 2013–2016 [22]. In another study, spatial and temporal trends of short-term health impacts of PM$_{1.5}$ in Iranian cities were estimated by AirQ+ modelling approach [21]. Despite these studies, estimation of IHD and stroke mortality attributed to air pollution have not been estimated yet. The aim of this study was to estimate the premature IHD and stroke deaths attributed to long-term exposure to PM$_{2.5}$ in 10 cities of Iran during March 2013 to March 2015 using AirQ+ model

**MATERIALS AND METHODS**

**Location and time**

Ten cities of Iran were chosen for a health impact assessment study about PM$_{2.5}$ exposure. These cities included Tehran, Mashhad, Isfahan, Shiraz, Tabriz, Ahvaz, Arak, Sanandaj, Khoram Abad, and Ilam. In addition, the study period included

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**AirQ+ software**

AirQ+ requires the following input data for a health impact evaluation: air quality data, total and at-risk population (over 25 years old, in case of IHD and stroke), baseline incidence of the interest health outcome i.e. IHD and stroke, a cut-off value for pollutants’ concentration, and Relative Risk (RRs) values if different from the default ones provided by WHO [19]. AirQ+ calculates different health-related estimates, including attributable proportion of cases, number of attributable cases, number of attributable cases per 100,000 at-risk population, proportion of cases in pollutant concentration range, and cumulative distribution by air pollutant concentration. These different estimates can be used in various ways depending on the assessment’s objectives [19].

**Air quality data**

Hourly concentrations of fine particulate matter were obtained from Department of Environment (DOE) of Iran. At first, zero and negative values were removed; then, daily concentrations were calculated just in monitoring stations that met APHEKOM and WHO’s criteria for health impact assessment of air pollution for Tehran and other cities, respectively [25, 26]. According to these criteria, only stations are valid that have more than 75% (APHEKOM) and 50% (WHO’s criterion) valid data in a year. In addition, the ratio of valid data in summer to winter or winter to summer should not exceed 2 [25]. Daily concentrations of PM$_{2.5}$ in the selected year was prepared to enter the AirQ+ model. In case of cities without PM$_{2.5}$ measurements, PM$_{10}$ concentrations were multiplied by a conversion factor of 0.5 to obtain PM$_{2.5}$ concentrations.

**Demographic data**

Age-specific population of each city was received from Statistical Centre of Iran. At-risk population (>25 years old) was calculated. Table 1 presents at-risk population for each city. Population of individuals older than 25 years in all the 10 cities were about 21 and 13 million, respectively.

**Baseline incidence (BI)**

Baseline incidence (BI) values for IHD and stroke mortality was obtained from Ministry of Health and Medical Education [27]. Due to lack of valid precise city-by-city information, the baseline incidence for all the 10 cities except for Tehran was assumed to be the similar. In addition, AirQ+ default relative risk (RR) values were used to evaluate the health impacts of PM$_{2.5}$ [28].

### Table 1. Population with age more than 25 years old during 2013-2015 period

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tehran</td>
<td>5662500</td>
<td>5805750</td>
</tr>
<tr>
<td>Mashhad</td>
<td>1622880</td>
<td>1733550</td>
</tr>
<tr>
<td>Isfahan</td>
<td>1287360</td>
<td>1321440</td>
</tr>
<tr>
<td>Shiraz</td>
<td>960000</td>
<td>1030000</td>
</tr>
<tr>
<td>Tabriz</td>
<td>977040</td>
<td>1035170</td>
</tr>
<tr>
<td>Ahvaz</td>
<td>700873</td>
<td>727512</td>
</tr>
<tr>
<td>Arak</td>
<td>338640</td>
<td>378950</td>
</tr>
<tr>
<td>Sanandaj</td>
<td>224200</td>
<td>237900</td>
</tr>
<tr>
<td>Khoram Abad</td>
<td>205440</td>
<td>230650</td>
</tr>
<tr>
<td>Ilam</td>
<td>102720</td>
<td>111000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12081653</strong></td>
<td><strong>12611922</strong></td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

Fig. 1 shows the average (± standard deviation) of PM$_{2.5}$ concentrations of 10 selected cities for this study. These concentrations are reported before [22, 24]. Highest average concentrations in the first year were observed in Ahvaz (62.61 ± 71.69), Isfahan (56.15 ± 28.73), and Arak (43.14 ± 34.26), respectively. Lowest average concentrations in the first year were observed in Ilam (28.78 ± 23.68), Sanandaj (29.78 ± 18.44), and Tabriz (30.68 ± 22.67), respectively. In case of the second year, the highest average concentrations were in Isfahan (54.99 ± 25.59), Ahvaz (53.09 ± 52.58), and Khoram Abad (41.02 ± 33.41), respectively. In addition, the lowest average concentrations in the second year were observed in Tabriz (17.23 ± 8.36), Shiraz (25.00 ± 10.41), and Ilam (26.04 ± 27.37), respectively.

Average concentrations of fine particulate matter in all the 10 cities were several times higher than the WHO's guideline value (10 μg / m$^3$) for annual PM$_{2.5}$ levels. The highest average concentrations in the first year were observed in Ahvaz, Isfahan, Arak, and Khoram Abad, respectively. The reason could be due to the occurrence of Middle Eastern dust storms in Ahvaz and Khoram Abad, and presence of large industries in Arak and Isfahan. In general, southern and western cities of Iran such as Ahvaz, Khoram Abad, etc. are faced to severe Middle Eastern dust storms in recent years. Very high concentrations of particulate matter have been reported for Ahvaz. Mean concentrations of TSP and PM$_{10}$ in Ahvaz were reported 1,481.5 and 1,072.9 μg / m$^3$ during dust storms, respectively [29]. This could be due to inappropriate water management and exacerbation of desertification in the surrounding areas [30]. The number of premature IHD and stroke deaths attributed to long-term exposure to PM$_{2.5}$ were estimated in 10 cities of Iran, including Tehran, Mashhad, Isfahan, Shiraz, Tabriz, Ahvaz, Arak, Sanandaj, Khoram Abad, and Ilam. The at-risk population was individuals aging more than 25 years old. This is based on the recent epidemiological studies and their meta-analyses that provide relative risk values for AirQ+ model.

Table 2 presents the estimated number of premature IHD and stroke deaths due to long-term exposure to PM$_{2.5}$ among individuals older than 25 years in 10 cities of Iran. In case of both IHD and stroke mortality, the highest number of IHD and stroke deaths was estimated to be in Tehran, Mashhad and Isfahan, respectively. On the other hand, the lowest number of premature IHD and stroke deaths attributed to PM$_{2.5}$ exposure were estimated to be in Ilam, Sanandaj, and Khoram Abad, respectively. The total number of IHD and stroke deaths in the March 2013-March 2014 and March 2014-March 2015 periods were 15479 and 15321 deaths, respectively.

The highest number of IHD and stroke deaths was estimated to be in Tehran, Mashhad and Isfahan, respectively. On the other hand, the lowest number of premature IHD and stroke deaths attributed to PM$_{2.5}$ exposure were estimated to be in Ilam, Sanandaj, and Khoram Abad, respectively. These results mainly reflect the amount of population in each city. For instance, the most deaths were estimated to be in Tehran. The high mortality in Tehran is driven by both its high population and high concentrations of PM$_{2.5}$. It is reported that about 70% of particulate air pollutants in Tehran were emitted from mobile sources during 2015 [31]. Therefore, a population-weighted index of mortality is required for better comparison between cities.

Table 3 shows the number of attributable IHD and stroke deaths per 100,000 population. In the first year, the most and least cases of IHD and stroke deaths per 100,000 population due to PM$_{2.5}$...
exposure were in Ahvaz and Ilam, respectively. In the second year, the highest and lowest number of IHD and stroke deaths were estimated to be in Isfahan and Tabriz, respectively. The average of excess IHD death due to exposure to PM$_{2.5}$ in all cities were 86 and 82 for the first and second years, respectively. In addition, the average of excess stroke deaths attributed to exposure to PM$_{2.5}$ in the first year and second year was 42 and 39 cases, respectively.

The results of estimated IHD and stroke deaths per 100,000 due to PM$_{2.5}$ concentrations were different from those raw estimated numbers for whole population. In case of deaths per 100,000, the most cases of deaths were estimated to be in cities (Ahvaz and Isfahan) where population are exposed to high concentrations of PM$_{2.5}$, despite the size of population. In addition to Ahvaz, other Western and Southern cities such as Khoram Abad and Sanandaj showed high number of deaths per 100,000. This is due to the occurrence of Middle Eastern dust storms (MED) – as a consequence of improper management of water resources - in recent years [30]. Mean concentrations of TSP and PM$_{10}$ in Ahvaz were reported 1,481.5 and 1,072.9 μg/m$^3$ during dust storms, respectively [29]. In another study during Middle Eastern dust storm period (April through September 2010) in Ahvaz, overall mean values of 319.6 ± 407.07, 69.5 ± 83.2, and 37.02 ± 34.9 μg/m$^3$ were monitored for PM$_{10}$, PM$_{2.5}$, and PM$_{1}$, respectively, with corresponding maximum values of 5338, 911, and 495 μg/m$^3$ [32, 33]. Various studies have indicated that the major source of particulate matter in Ahvaz is crustal dust [34 - 36].

The total number of IHD and stroke deaths in the March 2013-March 2014 and March 2014-March 2015 periods were 15479 and 15321 deaths, respectively. World Health Organization (WHO) have reported IHD and stroke mortality and burden of disease attributed to exposure to fine particulate matter (PM$_{2.5}$) for Iran in 2016. According to this report, years of life lost (YLL), disability-Adjusted Life Year (DALY), and number of IHD deaths attributed to PM$_{2.5}$ in Iran were 422105 years, 425114 years, and 16484 cases, respectively. In addition, YLL, DALY, and number of stroke deaths attributed to PM$_{2.5}$ in Iran were 180270 years, 183554 years, and 7290 cases, respectively [37]. These results are different from those obtained in the present study, mainly because this study considered only 10 cities of country with high population and more robust air quality dataset.

Table 2. Attributable number of IHD and stroke due to long- term exposure to PM$_{2.5}$ among individuals older than 25 years in March 2013 - March 2015

<table>
<thead>
<tr>
<th>Cities</th>
<th>IHD ((95% CI))</th>
<th>Stroke ((95% CI))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tehran</td>
<td>4851 (3642 - 6000)</td>
<td>4876 (3646 - 6033)</td>
</tr>
<tr>
<td>Mashhad</td>
<td>1360 (1016-1682)</td>
<td>1345 (988-1644)</td>
</tr>
<tr>
<td>Isfahan</td>
<td>1193 (919-1464)</td>
<td>1213 (929-1492)</td>
</tr>
<tr>
<td>Shiraz</td>
<td>781 (579-965)</td>
<td>778 (569-946)</td>
</tr>
<tr>
<td>Tabriz</td>
<td>785 (581-964)</td>
<td>689 (496-828)</td>
</tr>
<tr>
<td>Ahvaz</td>
<td>657 (507-803)</td>
<td>662 (507-815)</td>
</tr>
<tr>
<td>Arak</td>
<td>296 (223-366)</td>
<td>309 (229-382)</td>
</tr>
<tr>
<td>Sanandaj</td>
<td>179 (133-220)</td>
<td>189 (140-232)</td>
</tr>
<tr>
<td>Khoram Abad</td>
<td>168 (124-207)</td>
<td>200 (150-248)</td>
</tr>
<tr>
<td>Ilam</td>
<td>81 (60-100)</td>
<td>85 (62-104)</td>
</tr>
<tr>
<td>Total</td>
<td>10351 (7784-12775)</td>
<td>10346 (7716-12724)</td>
</tr>
</tbody>
</table>

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Despite the WHO report, no studies have been conducted to estimate the number of IHD and stroke deaths in Iran. However, other health outcomes are well documented. According to a study, it was reported that the total number of deaths attributed to PM$_{10}$, PM$_{2.5}$, O$_3$, NO$_2$, and SO$_2$ over these three years were 4192, 4336, 1363, 2830, and 1216, respectively. The mortality in March 2015 – March 2016 showed a reduction of 9 %, 38 %, 14 % in comparison to March 2013 – March 2014 for PM$_{2.5}$, O$_3$, NO$_2$, and SO$_2$, respectively. Cardiovascular mortality due to PM$_{10}$ was estimated to be 1075, 1100, and 1113 for each of the three years, respectively. Cardiovascular hospital admissions attributed to PM$_{10}$ were 2185, 2236 and 2262 cases for each of the three years, respectively. The sum of lung cancer deaths due to PM$_{2.5}$ exposure in each city was estimated. Despite the high number of lung cancer deaths in Tehran, higher AP values were observed in cities such as Isfahan, Ahvaz, Khoram Abad and Arak, reflecting the higher risk of death per unit of population [22].

In another study, total attributable short-term deaths due to PM$_{2.5}$ exposure during the three-year period in 10 cities of Iran were 3284 (95% CI: 1207-5244). The average daily premature deaths attributed to PM$_{2.5}$ were calculated to be 3 deaths per day. The highest number of premature deaths within the three-year period was estimated to be 548 in Tehran, largely reflecting mostly its population of nearly 9 million. The western and southern cities of Iran have occurrences of severe dust storms and showed high estimated rate of death attributed to air pollution. The health impacts in all cities have decreased in the third year compared to the first year except for Ahvaz, Khoram Abad, and Ilam [21]. In a study in Mashhad, the number of premature deaths due to short-term exposure to PM$_{2.5}$ was estimated to be 600 cases during 2014 - 2015 period [38]. Another study in Ahvaz showed that the number of mortality attributed to short-term exposure to PM$_{10}$ was 278 cases in 2014 [39.

<table>
<thead>
<tr>
<th>Cities</th>
<th>IHD (No. of attributable deaths)</th>
<th>Stroke (No. of attributable deaths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tehran</td>
<td>86</td>
<td>84</td>
</tr>
<tr>
<td>Mashhad</td>
<td>84</td>
<td>78</td>
</tr>
<tr>
<td>Isfahan</td>
<td>93</td>
<td>92</td>
</tr>
<tr>
<td>Shiraz</td>
<td>81</td>
<td>76</td>
</tr>
<tr>
<td>Tabriz</td>
<td>80</td>
<td>67</td>
</tr>
<tr>
<td>Ahvaz</td>
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<td>91</td>
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<tr>
<td>Arak</td>
<td>87</td>
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<tr>
<td>Sanandaj</td>
<td>80</td>
<td>79</td>
</tr>
<tr>
<td>Khoram Abad</td>
<td>82</td>
<td>87</td>
</tr>
<tr>
<td>Ilam</td>
<td>79</td>
<td>77</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>86</strong></td>
<td><strong>82</strong></td>
</tr>
</tbody>
</table>

Table 3. Attributable number of IHD and stroke deaths per 100,000 population due to long-term exposure to PM$_{2.5}$ among individuals older than 25 years in March 2013 - March 2015

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CONCLUSIONS

The number of premature deaths due to ischemic heart disease and stroke that are attributable to long-term exposure to PM$_{2.5}$ was estimated for 10 cities of Iran including Tehran, Mashhad, Isfahan, Shiraz, Tabriz, Ahvaz, Arak, Sanandaj, Khoram Abad, and Ilam. The results showed high IHD and stroke mortality due to PM$_{2.5}$ concentrations. Southern and Western cities showed high number of deaths per 100,000. Special considerations should be given to action plans for improving air quality in these cities. On the other hand, high-populated cities such as Tehran showed to have the most cases of estimated premature deaths. Any reduction in concentrations of PM$_{2.5}$ in Tehran can reduce the number of attributable deaths significantly. The results of this study indicated the necessity of urgent actions to improve the outdoor air quality in Iranian cities.

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COMPETING INTERESTS

The authors declare that they have no conflict of interest.

ACKNOWLEDGEMENTS

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ETHICAL CONSIDERATIONS

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.

REFERENCES


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