



An 8-year study of people with multiple sclerosis in Isfahan, Iran: Association between environmental air pollutants and severity of disease

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ABSTRACT

The evidence for an impact of ambient air pollution on the incidence and severity of multiple sclerosis (MS) is still limited. In the present study, we assessed the association between daily air pollution levels and MS prevalence and severity in Isfahan city, Iran. Data related to MS patients has been collected from 2008 to 2016 in a referral university clinic. The air quality index (AQI) data, were collected from 6 monitoring stations of Isfahan department of environment. The distribution map presenting the sites of air pollution monitoring stations as well as the residential address of MS patients was plotted on geographical information system (GIS).

An increase in AQI level in four areas of the city (north, west, east and south) was associated with higher expanded disability status scale (EDSS) of MS patients [logistic regression odds ratio = 1.01 (95% CI = 1.008, 1.012)]. Moreover, significant inverse association between the complete remission after the first attack with AQI level in total areas [logistic regression odds ratio = 0.987 (95% CI = 0.977, 0.997)] was found in crude model. However, after adjustment for confounding variables through multivariate logistic regression, AQI level was associated with degree of complete remission after first attack 1.005 (95% CI = 1.004, 1.006). The results of our study suggest that air pollution could play a role in the severity and remission of MS disease. However, more detailed studies with considering the complex involvement of different environmental factors including sunlight exposure, diet, depression and vitamin D are needed to determine the outcome of MS.

1. Introduction

Multiple sclerosis (MS) is a chronic neuroinflammatory disease of the central nervous system (CNS) that is characterized by myelin loss, axonal deterioration in focal areas of the CNS and developing neurological dysfunction (Dutta and Trapp, 2011). The disability of MS patients is quantified by expanded disability status scale (EDSS) which in more severe disability states the score is higher (Kurtzke, 1983). The etiology of MS remains evasive, nevertheless genetic, exogenous factors such as infectious, environmental or behavior have important roles, both independently and interactively, in disease susceptibility (Franklin and Nelson, 2003; Oksenberg et al., 1999; Dehghani et al., 2015).

A further increase in the number of incidences of MS has been observed in recent decades. Thus, it is of crucial importance to increase the understanding of the prevalence of MS and its relation to environmental triggers. The relevant environmental element(s) in MS

susceptibility is not yet known. However, among environmental factors; infectious agents, low levels of vitamin D and smoking have been associated with increased risk of developing MS (Ramagopalan et al., 2013; Ebers, 2008; Gourraud et al., 2012).

It has been proved that neuroinflammation plays a crucial role in MS pathogenesis. On the other hand, experimental and epidemiological studies have indicated adverse health effects of exposure to airborne particulate matter (PM) including neuroinflammation and the reserve of proteins associated with neurodegenerative diseases (Calderon-Garciduenas et al., 2008a; Pfau et al., 2008).

Some studies have shown that adverse effects of air pollution on central nervous system (CNS). However, it is not known exactly how exposure to ambient air pollution may affect the nervous system (Calderon-Garciduenas et al., 2002; Calderon-Garciduenas et al., 2004; Calderon-Garciduenas et al., 2008b). Also, the evidence for an impact of ambient air pollution on the incidence of MS is still limited. Oikonen

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et al. have been suggested a direct association between frequency of MS relapse and airborne particulate matter (PM) (Oikonen et al., 2003). In addition, Heydarpour et al. in an epidemiological study have shown a different exposure to airborne particulate matter (PM) in MS cases compared to matched controls (Heydarpour et al., 2014).

Isfahan is among the most polluted cities in Iran. This is partly attributable to its geography; high traffic density, massive steel mills and other industries (Borhan Mansouri, 2013). Therefore, the objective of present study was to estimate the association between air pollution level and MS prevalence and severity in Isfahan city, Iran.

2. Materials and methods

2.1. Study area

This cross-sectional study was conducted in Isfahan, Iran, which is located between 30°42' and 34°30' N latitude and 49°36' and 55°32' E longitude. According to the 2011 national census, the population of Isfahan province was 3.8 million. The town is located on Zayanderud River plain at the foothills of the Zagros mountain range. It is the most industrialized city of Iran, not only by the existence of heavy industries but also with the establishment of electricity and natural gas to most parts of the province.

2.2. Multiple sclerosis data

Data related to MS patients has been collected by Kashani hospital MS clinic, Isfahan, Iran from 2008 to 2016. Briefly, MS clinics in Isfahan use standardized, personally administered questionnaires to screen individuals with MS and to collect data about themselves and their families.

More than 2000 patients have included in this society according to fulfilling McDonalds' criteria for MS or the Poser criteria (McDonald et al., 2001). In total 1170MS patients fulfilled the criteria and after obtaining informed consent, patients are asked to complete structured questionnaire. The first neurological examination was done at registration time that was during first 6 months.

The data collectors assessed the degree of MS disability by using the EDSS (Kurtzke, 1983) and the degree of remission after the first attack. The assessment of the degree of MS disability and the degree of remission was verified by a senior neurologist who specifically confirmed the assessments of EDSS and remission through the medical records. The degree of remission in most cases was evaluated between 2 and 3 months after neurologic episode and complete remission was detected as disappearing the clinical symptoms that was reported by patient. Also, the duration of disease was from one year to 15 years.

2.3. Measurements

Age was assessed as a continuous variable. Sex ratio F:M was 3.89 and the mean age was 38.05 ± 16.27 years. Marital status was categorized as single, married, widowed/ divorced. Three levels of education were created: illiterate less than high school more than high school. Employment status was categorized as employed and unemployed. Participants were asked whether they had ever received a depression diagnosis by a physician. If a participant had reported a physician diagnosis of depression he/she was classified as depressed and otherwise, he/she was considered as non-depressed. Also, the patients were classified as smokers and non-smokers.

Data on the air quality index (AQI) were obtained from the Isfahan Department of Environment, which is a governmental organization and collects data from all air pollution-monitoring sites of the city using the same standards and equipment. The mean AQI values from the study time till one year prior to the survey were used in this study. These data were obtained from the North, South, Central, East, and West parts of the Isfahan city by considering the concentration of air pollutants of all

provincial counties containing different clusters. The Expanded Disability Status Scale (EDSS) was assessed during inclusion and categorized as (< 3.5 and > 3.5). EDSS was categorized regard to moderate disability (in EDSS > 3.5 the patient can walk without aid but not > 500 m) and it was assessed during inclusion. The degree of remission after the first attack was considered as two categorizes (partial remission and complete remission). We evaluate the patient's data and air pollution during all of the seasons so seasonal data was not important in our study.

2.4. Air pollution data

The AQI is an index for reporting daily air quality. It shows how clean or polluted the air is, and proposes its associated health effects. The AQI focuses on health effects that may be experienced within a few hours or days after breathing polluted air. EPA calculates the AQI for five major air pollutants regulated by the Clean Air Act: ground-level ozone, particulate matter, carbon monoxide, sulfur dioxide, and nitrogen dioxide. For each of these pollutants, EPA has established air quality standards to protect public health.

EPA has assigned a specific color to each AQI category to make it easier for people to understand quickly whether air pollution is reaching unhealthy levels in their communities. For instance, the color orange means that conditions are "unhealthy for sensitive groups," while red means that conditions may be "unhealthy for everyone".

Air pollution data for 8 years (2008–2016) collected from 6 monitoring stations of Isfahan department of environment, at which criteria pollutants (e.g., O₃, NO_x, CO, SO₂, PM₁₀, and PM_{2.5}) were routinely measured. Air pollution has natural and anthropogenic (man-made) sources which are mostly related to the burning of multiple types of fuel. Six of the most common air pollutants are known as criteria air pollutants including ozone, particulate matter (PM), carbon monoxide (CO), sulfur dioxide (SO₂), lead, and nitrogen dioxide (NO₂). Air quality index (AQI) is based on daily measurement of all criteria pollutants except lead.

We used air quality index (AQI) data, which reported daily by Isfahan department of environment. Air pollution stations located in different parts of the city including North, West, South, and East (Fig. 1). We used interpolation method, and for some points between two air monitoring stations we used average of two stations concentration.

2.5. Distribution map

Geographic Information Systems (GIS) is a crucial scientific tool for health data processing, analysis of geographical distribution and variation of diseases, mapping, monitoring and managing health epidemics.

In the present study, Arc GIS 9.3 software was used to prepare the distribution map presenting the sites of air pollution monitoring stations as well as the residential address of MS patients (Fig. 1). We used AQI level of monitoring stations in different parts of city and linked it to MS patient's address. The daily data for each monitoring station were used for determination of annual average concentrations.

Isfahan has two main factories including Mobarakeh Steel Company and Isfahan Steel Company (Zob Ahan). Both of these companies located in south west of Isfahan. The map presented in this manuscript relates to the city of Isfahan, and since these two factories are located around the city, it was not possible to display them on the map. Wind speed annual average in Isfahan is 2.5 m/s. Wind direction in year is mostly from west. Maximum annual wind speed is from 1951 to 2015 (m²/s) (Fig. 2).

2.6. Statistical analysis

All data were summarized and displayed as mean (\pm standard

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