Investigating the relationship between the long-term exposure to air pollution and the frequency of depression in Shiraz during 2010-2017

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Abstract
Background: Exposure to environmental pollutants which have entered the atmosphere due to human and industrial activities results in harmful and unwanted effects on human health. The undesired effects of air pollution on mental disorders, mortality, and psychological disorders have been proven. Depression is a common mental health problem in today’s societies which impacts the quality of life. The objective of this study was to determine the relation between exposure to air pollution and frequency of depression in Shiraz (Southern Iran).

Methods: Archived documents of 2658 patients diagnosed with major depressive disorder (MDD) from a psychiatric university hospital were reviewed. The concentrations of five air pollutants including CO, NOX, O3, PM10, and NO2 were determined daily in two air quality monitoring stations in downtown Shiraz (Imam Hossein Square) and Kazeroon Gate. The data relevant to these five pollutants were gathered every day for 83 months, from 2010 to 2017, and for more precision, the mean values were used. The relationship between the concentration of each pollutant in the air and the number of patients referring to hospital was determined using the Spearman’s correlation coefficient.

Results: There was a direct and significant relationship between all pollutants and the number of hospital admissions in each month (P<0.05) except for CO which did not show a significant relationship with hospital admission due to depression (P>0.05).

Conclusion: The results of this study indicated a positive relationship between air pollution and depression. Of course, to prove this relationship, it is essential to conduct a number of studies with appropriate methodology and design.

Keywords: Air pollutant, Environmental exposure, Inhalation exposure, Mental disorders, Depression

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Introduction
Different kinds of pollutants enter the atmosphere from natural resources or due to human and industrial activities (1,2), and exposure to each of these pollutants can result in unwanted and harmful effects on human health (3-6). Different studies illustrated that air pollution can significantly increase the risk of respiratory disease (7-9), cardiovascular events (10), cancer, stroke, and type 2 diabetes mellitus (11). Moreover, the adverse effects of air pollution on brain disorders and mortality have been proved (12).

Depression is a common mental health problem in
today’s societies which impacts the quality of life and has a significant burden on healthcare systems. Although depression is one of the main reasons for committing suicide, medications and non-psychological diseases such as stroke, diabetes, and cancer can be the attributing factors (4,13,14). Epidemiological studies have shown a relationship between air pollution and depression symptoms in humans (15,16).

In a study by Joubert et al, a significant relation between NO\textsubscript{x} and depression was determined (3). Joubert et al proved that depression symptoms and atmospheric pollution increase the risk of stroke (4). In a study by Vert et al on long and short-term exposure to air pollutants and also anger and depression, it was indicated that the increase in pollutant concentration increases anger and depression symptoms (12). Cho et al studied the relationship between air pollution, depression and heart disease and showed that increasing PM\textsubscript{10}, SO\textsubscript{2}, NO\textsubscript{x}, and CO concentration enhances depression symptoms effectively and significantly (13). In the research by Lamers et al in the USA, it was determined that long and short-term exposure to air pollution increases the stress symptoms that are mostly accompanied by depression (17).

Since the air quality in metropolitan cities such as Shiraz is declining over time and many studies have emphasized the relationship between air pollution and diseases and given that limited epidemiological studies have been performed to evaluate these issues in Middle Eastern countries, this study aims to determine the relationship between depression and exposure to air pollutants in Shiraz (as a developing and industrialized metropolis, Iran from 2010 to 2017).

Materials and Methods

Study design and population

This cross-sectional study was conducted on 2658 patients diagnosed with major depressive disorder (MDD) based on the criteria proposed by Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (American Psychiatric Association, 2000). The data were collected from patient documents in a psychiatric university hospital in South of Iran, from April 2010 to February 2017. Informed consent was obtained from all participants and from the parents of the participants under 18 years of age.

The inclusion criteria were (a) having normal cognition, (b) being 16-87 years old, and (c) being diagnosed with MDD by a faculty psychiatrist. The exclusion criteria were (a) being of a cognitive performance that falls outside the established cut-offs, and having (b) significant diseases that could interfere with cognition, (c) severe auditory, visual, neurodevelopmental, and/or psychomotor disorders, (d) brain injury, and (e) other major active psychiatric disorders according to the criteria proposed by DSM-IV-TR (American Psychiatric Association, 2000), including schizophrenia, dementia, or bipolar disorders.

All methods were carried out in accordance with relevant guidelines and regulations and all experimental protocols were approved by Ethics Committee of Shiraz University of Medical Sciences.

Air pollution assessment

This was a cross-sectional study. The concentrations of five air pollutants including CO, NO\textsubscript{x}, O\textsubscript{3}, PM\textsubscript{10,} and NO\textsubscript{2} were determined daily in two air quality monitoring stations in downtown Shiraz (Imam Hossein Square) and Kazeroon Gate. These stations are under the supervision of the Environmental Health Organization. The data regarding these five pollutants were gathered every day for 83 months, between 2010 and 2017, and for more precision, their mean values were used.

Quality control was conducted by duplicate samples methods. For this method, two out of every few samples were taken side by side using the same procedures and tested separately and analyzed in the same procedure.

Statistical analysis

The normal distribution of air pollutants and the number of hospital visits were examined before analyzing the data using the Kolmogorov-Smirnov test. The results of this test showed that none of the variables had a normal distribution \((P < 0.05)\). The mean value of each air pollutant per month as well as the number of patients in that month were available. As a result, the Spearman’s correlation coefficient was used to determine the relationship between the concentration of each pollutant in the air and the number of patients that referred to hospital (data on the number of patients and the concentration of air pollutants did not have a normal distribution and Spearman’s correlation coefficient was used).

One of the limitations of the present study was that only data on the mean of each air pollutant and the number of depressive patient admissions were available monthly and the access to other information (such as confounders) was limited.

Results

Population characteristics

A total of 2364 depression cases were recorded during 3636 days from 2010–2017, of which 1551 cases (65.60%) were men and 813 cases (34.40%) were women. The average age of the participants was 38.85±13.67.

Air pollution and depression

This was the first study to investigate the relationship between long-term exposure to air pollution and depression in Shiraz. The data regarding air pollution from April 22, 2010 to March 20, 2017 and the number of hospital admissions due to depression were evaluated. Annual mean concentration of air pollutants and total number of depression hospital admissions are presented in Table 1 and Figure 1.
As it is depicted in Table 1, the mean concentration of PM\(_{10}\) and NO\(_X\) increased from 2010 to 2017. The mean concentration of CO and O\(_3\) increased until 2015 and then decreased.

The correlation coefficient between the concentration of air pollutants and the number of hospital admissions due to depression in each month in Shiraz are presented in Table 2.

The results revealed that all pollutants had a direct and significant relationship with the number of hospital admissions in each month (\(P<0.05\)) except CO which did not have a significant relationship with hospital admissions due to depression (\(P>0.05\)). On the other hand, as the mean value of pollutants increased each month (except CO), the number of hospital admissions due to depression also increased.

### Discussion

Some studies in Seoul, Canada and United State emphasize the relationship between air pollution and depression in different countries (13,16,18,19). In the study by Vert et al, the investigation of the effect of long-term exposure to air pollution on stress and depression showed that the increase in the level of air pollutants had a direct and positive relationship with depression. Their results indicated that there was a higher possibility of depression with increasing exposure to NO\(_X\), NO\(_2\), PM\(_{10}\), and O\(_3\), which is similar to the results of the present study (12). Another study on American women showed that the increase in O\(_3\) and PM\(_{10}\) increased depression (20). A research done in China showed that increasing PM\(_{2.5}\) concentration caused enhancement of symptoms of depression. It is noticeable that neighborhood and social capital decreased the negative effects of PM\(_{2.5}\) on depression symptoms among examined persons (21). Various studies have described different biological reasons for this issue. More air pollution can increase the risk of cardiovascular effects and these diseases are related to depression symptoms (22,23). Therefore, residents of cities with more air pollution have higher risks of cardiovascular diseases and depression, thus, there was observed a relationship between air pollution, depression symptoms, and cardiovascular effects. Besides, air pollution can decrease physical activities and sports in polluted outdoors and consequently results in depression symptoms (21-24). Moreover, air pollution biologically

| Year | Number | O3 (ppm) | NOX (ppm) | NO2 (ppm) | NO (ppm) | PM\(_{10}\) (µg/m\(^3\)) | CO (ppm) |
|------|--------|----------|-----------|-----------|---------|-----------------|---------|
| 2010 | 23     | 0.02 (0.008) | 0.08 (0.02) | 0.02 (0.001) | 0.04 (0.01) | 99.67 (32.23) | 2.31 (0.63) |
| 2011 | 18     | 0.02 (0.008) | 0.06 (0.01) | 0.02 (0.003) | 0.03 (0.01) | 80.90 (19.32) | 1.55 (0.27) |
| 2012 | 167    | 0.02 (0.008) | 0.05 (0.01) | 0.02 (0.003) | 0.03 (0.008) | 92.44 (32.88) | 1.45 (0.23) |
| 2013 | 415    | 0.16 (0.02) | 3.89 (13.28) | 4.76 (13.16) | 6.79 (15.30) | 44.53 (27.80) | 0.95 (0.56) |
| 2014 | 492    | 33.39 (43.21) | 9.99 (17.66) | 9.61 (16.98) | 4.57 (3.67) | 70.72 (23.84) | 0.86 (0.49) |
| 2015 | 568    | 32.76 (37.43) | 24.13 (9.31) | 14.98 (4.81) | 18.79 (15.58) | 52.54 (13.20) | 5.66 (5.69) |
| 2016 | 556    | 31.30 (17.91) | 29.09 (8.20) | 3.98 (2.47) | 25.34 (7.49) | 30.70 (7.77) | 3.07 (0.67) |
| 2017 | 125    | 29.02 (2.44) | 33.48 (9.55) | 9.25 (8.69) | 30.52 (6.40) | 25.75 (2.47) | 3.61 (0.03) |

Dare are expressed as mean (standard deviation).

| Hospital visit | CO (ppm) | O3 (ppm) | NOX (ppm) | NO2 (ppm) | NO (ppm) | PM \(_{10}\) (µg/m\(^3\)) |
|----------------|---------|----------|-----------|-----------|---------|-----------------|
| Correlation coefficient | 0.129 | 0.715 | 0.494 | 0.660 | 0.652 | 0.564 |
| P value | 0.246 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |
may decrease sunlight that may be a stressor for residents’ nervous system that results in depression (25-27). Some studies have shown that air pollution can decrease face-to-face social contact among neighbors, therefore, the danger of depression enhances (28-30). In a study by Cho et al. a positive and significant relationship was reported between SO$_2$, PM$_{10}$, NO$_3$, and CO and admission to Seoul hospital for depression. They announced that PM$_{10}$ might induce dopamine neuron damage causing changes in neurotransmitter levels via an inflammatory process (13). Moreover, in a cohort study on South Korean adults, it was proved that long-term exposure to air pollutants such as PM$_{10}$ and NO, increases suicide due to depression (31). Indeed, inhalation of PM can activate pro-inflammatory cytokines in human macrophages, initiating an inflammatory response and inducing oxidative stress (32-36). Eventually, oxidative stress and systemic inflammation can cause depression and anxiety behaviors (37,38). Dorado-Martínez et al demonstrated that O$_3$ can act as an oxidative stress factor and finally results in brain damage and sudden severe depression symptoms which can lead to committing suicide (39). Nevertheless, some studies show different results. For example, the results of a study in Canada showed that the relationship between air pollution and depression in people over 65 years old was not significant (19). But, some study shows there are relationship between air pollution and other disease such as cardiovascular disease (7).

**Limitations and strengths**

In this study, a large and representative dataset was evaluated for a long period of time. The study was restricted to analyze cases referring to the emergency department (ED) that were acute and relatively severe. This data also reflects where symptoms were initiated or exacerbated, therefore, it was limited compared to other types of medical care.

ED cases for depressive episodes might have various psychiatric symptoms other than depression such as anxiety, suicidal ideation, and psychosis, and it is possible that air pollution might trigger those conditions as well. Patients might have had other comorbidities which were not documented.

**Conclusion**

The present study showed a significant and effective relationship between air pollution and the possibility of depression. Nonetheless, in order to prove the causal relationship between air pollution and depression, further researches with suitable methods are required.

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**Ethical issues**

All methods were carried out in accordance with relevant guidelines and regulations and all experimental protocols were approved by Ethics Committee of Shiraz University of Medical Sciences. This research has been approved by the Ethics Committee of Shiraz University of Medical Sciences, Iran (number: ir.iums.rec.1393.8095)

**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

Data collection, analysis, and interpretation were accomplished by contribution of all authors, and the authors reviewed, revised, and approved the manuscript as well.

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