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Relationship Between the Incidence of Pulmonary Embolism and the Quantitative Level of Air Pollution (NO_2, SO_2, CO, O_3, and PM_{10}) in Patients Referred to Mashhad Hospitals in 2019

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Abstract

Background: Air pollution is known to be associated with increased levels of inflammatory markers, vascular endothelial damage, and alterations in blood coagulation factors. It represents one of the most significant environmental hazards in urban areas, with adverse effects on the health of the population.

Objectives: This study aimed to investigate the relationship between the incidence of pulmonary embolism (PE) and the quantitative levels of various air pollution parameters.

Methods: In this descriptive-analytical (cross-sectional) study, we examined all patients diagnosed with PE who were referred to Ghaem and Imam Reza (AS) Hospitals in Mashhad during the year 2019. Daily data on each air pollutant, including NO_2, SO_2, CO, O_3, and PM_{10}, were obtained from the Meteorological Center. For each patient's assessment, we considered the average pollution levels over the past 30 days. The collected data were subsequently analyzed using independent samples t-tests and the Mann-Whitney U test in SPSS 22.

Results: The findings of this study revealed a statistically significant association between elevated levels of PM_{10} and O_3 and the occurrence of PE. However, no such relationship was observed for NO_2 and CO in relation to the risk of PE.

Conclusions: It can be concluded that increased levels of PM_{10} and O_3 are linked to a higher risk of developing PE, while other pollutants showed no evidence of association in this study.

Keywords: Pulmonary, Embolism, Air Pollution

1. Background

Acute pulmonary embolism (APE) represents a common and potentially fatal type of venous thromboembolism (VTE) (1, 2). An analysis of databases revealed a doubling in the incidence of pulmonary embolism (PE), increasing from 62 cases per 100 000 individuals in the five years before 1998 to 112 cases per 100 000 in the seven years following 1998 (3).

Air pollution refers to an elevated and heterogeneous mixture of gases, liquids, and fine suspended particles. These particles include carbon monoxide (CO), nitrogen oxides, sulfur dioxide, ozone, fine particles with a diameter of less than 10 µm, and very small particles

with a diameter of less than 2.5 µm (4). Reports from the World Health Organization (WHO) highlight that air pollution ranks among the top ten risk factors contributing to global mortality, causing approximately 7 million deaths worldwide each year (5-7). It is worth noting that air pollution is responsible for roughly 800 000 premature deaths annually, attributed to cardiovascular disease, respiratory issues, and lung cancer (8).

Studies and reports from the WHO indicate that air pollutants have exceeded permissible limits in 50 countries. In Iran, emissions of these air pollutants have reached dangerous levels in cities like Tehran, Mashhad, and Isfahan (9). Disturbingly, more than 43 000 individuals in Iran lose their lives every year due to heart attacks and respiratory failures (10). According to reports by the World Bank in 2005, the damage inflicted by air pollution in Iran is equivalent to 60% of the country's gross domestic product (11). Given these factors, air pollution stands as one of the most significant natural hazards in urban areas, and its effects are a prominent focus in climate studies (12).

On the other hand, some studies have suggested that air pollution is associated with an increase in inflammatory markers, vascular endothelial damage, and alterations in blood coagulation factors, including platelet adhesion and thrombin production. Several studies have explored these mechanisms in relation to the impact of air pollution on acute coronary heart diseases. However, limited research has been conducted on the connection between air pollution and thromboembolism, as well as its underlying mechanisms.

The city of Mashhad is the second most populous city in the country, following Tehran, and ranks second in terms of metropolitan area size (13). Additionally, it is one of the largest religious cities globally, attracting a significant number of pilgrims and travelers each year (14). Air pollution poses a significant environmental challenge in the country, and existing studies on the relationship between air pollution and the health of Iranian society are scarce.

2. Objectives

This study aimed to investigate the association between the incidence of PE and the levels of air pollution among patients referred to hospitals in Mashhad in 2019.

3. Methods

In this descriptive-analytical (cross-sectional) study, after receiving approval from the Ethics Committee of Zahedan University of Medical Sciences (IR.ZAUMS.REC.1400.084), we conducted research on patients diagnosed with PE through lung CT angiography. These patients were referred to Ghaem and Imam Reza (AS) Hospitals in Mashhad during the year 2019.

During 2019, a total of 3 542 patients who had a history of acute shortness of breath and were suspected of having PE were referred to Mashhad hospitals. CT angiography was performed on these patients to confirm the diagnosis of PE. Among these patients, 736 received a positive diagnosis for PE. However, we excluded 54 cases with a history of pregnancy, 45 cases with a previous history of PE, 11 cases with a recent history of prolonged travel, and 5 cases with a history of hormone therapy. Therefore, our study focused on 708 patients with pulmonary thromboembolism in Mashhad Hospitals. We collected information related to daily air pollutant levels from the local meteorological center.

We extracted demographic information, such as age and gender, from their medical records. If necessary, we contacted the patients to gather additional information. The patients were also questioned about potential risk factors for PE, including a history of venous thrombosis, recent surgeries, immobility, recent traumas within the last month, hormone therapy, pregnancy, extended periods of travel (more than 4 hours a week before their visit), active malignancy, and chemotherapy treatments. Patients with a positive history in any of these cases were excluded from the study.

Meteorological parameters were also gathered from the air quality control station closest to the patient's residence. Information regarding the levels of each air pollutant (NO_2, SO_2, CO, O_3, and PM_{10}) was collected on a daily basis from the meteorological center of the city. The average meteorological data for the past 30 days were taken into account when each patient was referred to the hospital. The study days were categorized into two groups based on the diagnosis of PE patients on those days: PE-positive days (days when embolism was reported) and PE-negative days (days when embolism was not reported). The data were entered into the statistical software SPSS version 22. Descriptive data (mean, standard deviation, frequency, and percentage) were examined using central and dispersion indices. Comparisons of means were carried out using independent *t*-tests or Mann-Whitney tests, as well as one-way analysis of variance or Kruskal-Wallis tests and chi-square tests, all at a significance level of 0.05.

4. Results

The average air pollutant levels for the past 30 days were calculated for all study days. The study days were categorized into two groups based on the diagnosis of PE: PE-positive days and PE-negative days. Subsequently, a comparison was made between these two groups regarding the 30-day average air pollutant levels. A statistically significant difference was observed between the two groups concerning the 30-day average PM_{10} levels. On days when patients were diagnosed with PE, there was a higher 30-day average PM_{10} level compared to other days ($P < 0.05$) (Table 1). While there was no statistically significant difference between the groups in terms of the average O_3 levels over the last 30 days, the P-value of 0.058 was very close to the significance criterion, suggesting that an increase in O_3 levels might not be entirely ineffective in the occurrence of PE (Table 1). However, no statistically significant relationship was found between the average levels of NO_2, CO, SO_2, and the incidence of PE over the last 30 days (Table 1).

Table 1. Average Levels of Air Pollution Particles in the Last 30 Days Before the Patients' Hospitalization Due to Pulmonary Embolism (PE) Diagnosis

Air Pollution Particles and Group	30 Days Before the Patients' Hospitalization	P-Value
PM_{10}, $\mu g/m^3$		0.04
Positive PE days	51.28 ± 16.22	
Negative PE days	46.64 ± 15.31	
O_3, $\mu g/m^3$		0.58
Positive PE days	31.14 ± 10.37	
Negative PE days	33.82 ± 10.18	
NO_2, $\mu g/m^3$		0.489
Positive PE days	32.76 ± 9.56	
Negative PE days	33.77 ± 9.98	
CO, $\mu g/m^3$		0.973
Positive PE days	1.89 ± 0.12	
Negative PE days	1.90 ± 0.13	
SO_2, $\mu g/m^3$		0.953
Positive PE days	15.86 ± 10.05	
Negative PE days	16.91 ± 10.80	

Table 1 showed that amongst all the air population particles, only PM_{10} was significant such that its averages were 51.28 ± 16.22 $\mu g/m^3$ and 46.64 ± 15.31 $\mu g/m^3$ for positive and negative PE days, respectively ($P = 0.040$).

Regarding gender, there were 366 (51.7%) male and 342 (48.3%) female patients. The average age of the patients was 58.83 ± 9.31 years. There was no statistically significant difference in average age between the two genders ($P = 0.73$).

5. Discussion

In recent times, the rapid advancement of technology and the increasing pace of urbanization in industrial regions have resulted in a significant rise in air pollution and global climate change (15, 16). This phenomenon poses a direct threat to public health, contributing to respiratory and cardiovascular diseases, such as asthma, allergies, acute bronchitis, cardiac arrhythmia, pneumonia, pulmonary fibrosis, venous thrombosis, and cancer (17-19). The current study aims to investigate the relationship between the incidence of PE and the quantitative levels of air pollution parameters (NO_2, SO_2, CO, O_3, and PM_{10}) among patients referred to hospitals in Mashhad and Zahedan in 2019. The key findings of this investigation include the following: (1) A significant association between elevated levels of PM_{10} and O_3 with the occurrence of PE; and (2) no significant relationship observed between SO_2, NO_2, CO, and the incidence of PE. According to the results of the present study, there is a significant association between upregulated levels of PM_{10} and O_3 and PE. Consistent with this study, other studies have reported that both animal and human studies indicate that exposure to air pollution increases the risk of thrombosis. Cardiovascular risk factors resulting from particulate air pollution encompass various factors, such as an increase in mean arterial blood pressure at rest due to heightened sympathetic tone or modulation of systemic vascular tone (20). It can also lead to an elevated risk of intravascular thrombosis through a transient rise in plasma viscosity and endothelial dysfunction (21), as well as the initiation and progression of atherosclerosis (22, 23). Furthermore, Colais et al. have highlighted those mechanisms predisposing individuals to thrombosis are activated following exposure to air pollution. They have also noted that long-term exposure to PM_{10} is associated with an increased risk of deep vein thrombosis (24). In accordance with our findings, Colais et al. conducted a study on hospitalized patients diagnosed with venous thrombosis or PE, concluding that the PM_{10} pollutant is linked to a heightened risk of PE (24). Additionally, Kacem et al. have indicated that PM_{10} pollutants play a role in the development of PE, aligning with the results of our study (25).

Miao et al. also explored the connection between air pollutants and PE, suggesting that O_3 can elevate the risk of PE. In our current study, the average O_3 level over

the last 30 days did not exhibit a significant association with PE. However, the proximity of the P-value (P = 0.058) to the significance threshold suggests that an elevated level of O_3 may still have some influence on the occurrence of PE (26). Consequently, based on our findings, heightened levels of PM_{10} and O_3 pollutants are linked to an increased risk of PE. Nevertheless, no compelling evidence emerged to support a relationship with the other pollutants examined in this study.

However, concerning NO_2, SO_2, and CO, our study did not discover any evidence of a relationship between these pollutants and an increased risk of PE. In a similar vein, Bumroongkit et al. investigated the correlation between air pollution and the prevalence of APE in Northern Thailand, finding no significant association between SO_2, NO_2, and CO with APE (21). In contrast, de Miguel-Diez et al. conducted an analysis and multiple comparisons to confirm the possible correlation between the study period and the annual average of the NO_2 factor, which showed a significant relationship, differing from our findings (27).

Other studies have produced contradictory results. For instance, some have reported a significant correlation between short-term NO_2 exposure and an increased risk of PE while finding no such correlation with PM_{10} and O_3, as observed in the study by Colias et al. (24). Furthermore, a meta-analysis conducted by Maio et al. suggested that SO_2, CO, PM_{10}, and $PM_{2.5}$ levels do not exhibit a significant relationship with PE (26). These discrepancies may arise from various study protocols, the presence of different confounding factors in distinct studies, the limited number of analyzed pollutants, and variations in geographical and climatic conditions.

Several limitations are worth noting in our study, including the restricted number of analyzed pollutants, the absence of meteorological parameters (such as temperature, humidity, and wind speed), and the omission of occupational status from the analysis, which should be considered as a potential confounding factor.

Footnotes

Authors' Contribution: Study concept and design: MK. M., and H. H.; analysis and interpretation of data: A. T. and F. H.; drafting of the manuscript: M. CH.; critical revision of the manuscript for important intellectual content: NA. M. and A. P.

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Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

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