

# Associations Between Air Pollution and Emergency Department Visits for Ischemic Stroke, Respiratory and Cardiovascular Diseases, in Izmir

*İzmir ilinde, hava kirliliği ile iskemik inme, solunumsal ve kardiyovasküler hastalıklara bağlı acil başvuruları arasındaki ilişki*

Türkiye Acil Tıp Dergisi - Turk J Emerg Med 2010;10(1):2-6

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## SUMMARY

**Objectives:** Some recent studies have shown that increased levels of particulate air pollutants are positively associated with cardiovascular morbidity and mortality, asthma, stroke and deep vein thrombosis. We aim to determine the association between levels of ambient particulate air pollutants and Emergency Department (ED) visits for ischemic stroke, cardiovascular and pulmonary disease in winter months.

**Methods:** This is a dual-center retrospective study. We identified adults patients who had been presented to emergency department with cardiovascular and pulmonary disease between October 1, 2008 and March 31, 2009. The air pollutants that were analyzed for this study included PM10, carbon monoxide (CO) and sulfur dioxide (SO<sub>2</sub>). For 6 months, air pollution data for downtown Izmir were obtained from the National Air Quality Monitoring system. Multiple linear regression was used to estimate for the effects of particulate air pollution factors and Rho Spearman test for the correlations between ED visits.

**Results:** There were 3070 cardiovascular and pulmonary disease of ED visits. We found no association between outdoor measures of CO, SO<sub>2</sub>, PM10 and COPD, heart failure and ischemic stroke visits. Significant correlations were found between ED visits for asthma and the mean ambient concentrations of CO (p=0.024, R<sup>2</sup>=%70) measurements and PM10 (p=0.024, R<sup>2</sup>=%70). Statistically significant associations were observed between pulmonary embolus and PM10 (p=0.016, R<sup>2</sup>=%55) with multiple linear regression. And statistically significant associations were observed between angina/myocardial infarction and CO (p=0.001) and SO<sub>2</sub> (p=0.005) with bivariate correlation.

**Conclusions:** An increase in ambient levels of CO is associated with an increase in the number of ED visits for MI and asthma. PM10 were strongly associated with pulmonary embolus and asthma visits during the warm season.

**Key words:** Air pollution; emergency department visit; ischemic stroke; respiratory and cardiovascular diseases.

## ÖZET

**Amaç:** Son zamanlarda yapılan bazı çalışmalarda, hava kirliliğine neden olan partiküler madde ve gazların artması ile kardiyovasküler mortalite ve morbidite, iskemik inme, astım ve derin ven trombozu gelişmesi arasında pozitif ilişki olduğu tespit edilmiştir. Bu çalışmanın amacı, kış aylarındaki havadaki partiküler kirlilik ile acil servise iskemik inme, kardiyovasküler ve pulmoner hastalıklar nedeni başvuran hastalar arasında ilişkiyi değerlendirmektir.

**Gereç ve Yöntem:** İki merkezin dahil edildiği bu retropektif çalışmada, hava kirliliğinin en yoğun hissedildiği kış aylarında, 1 Ekim 2008 ve 31 Mart 2009 tarihleri arasındaki periyotta, acil servise kardiyovasküler ve pulmoner hastalıklar nedeni ile başvuran erişkin hastalar değerlendirildi. Ulusal hava kalitesi izleme ağından elde edilen hava kirliliği parametreleri olan hava asılı partiküler materyaller (PM10), kükürtdioksit (SO<sub>2</sub>) ve karbonmonoksit (CO) ölçümlerinden elde edilen değerlerin ikişer haftalık periyodlardaki ortalamaları ile acil servis başvuruları arasındaki ilişki çoklu lineer regresyon analizi ve Rho Spearman korelasyon ile değerlendirildi.

**Bulgular:** Kardiyovasküler ve pulmoner hastalıklara bağlı 3070 başvuru tespit edildi. Kent merkezindeki dış çevre ölçümlerinden elde edilen SO<sub>2</sub>, CO, PM10 değerleri ile acil servise başvuran KOAH, kalp yetmezliği ve iskemik inme başvuruları arasında istatistiksel olarak anlamlı bir ilişki olmadığı görüldü. Çoklu regresyon analizinde, CO seviyesindeki yükselme ile başvuran astımı olan hasta sayısı arasında pozitif ilişki bulundu (p=0.024, R<sup>2</sup>=%70). Ayrıca PM10 değerlerinin artışı ile astım (p=0.024, R<sup>2</sup>=%70) ve pulmoner emboli (p=0.016, R<sup>2</sup>=%55) başvuru sayısı arasında

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daki istatistiksel ilişki anlamlı olarak yüksek bulundu. Bivaryans korrelasyon analizinde, anjina/miyokardiyal enfarktüs başvuruları ile CO ( $p=0.001$ ) ve SO<sub>2</sub> ( $p=0.005$ ) düzeyleri arasındaki ilişki, istatistiksel olarak anlamlı tespit edildi.

**Sonuç:** Dış ortamdaki hava kirliliğine neden olan CO artışı, miyokardiyal enfarktüs ve astım hasta sayısını arttırmaktadır. Kış aylarında PM10 konsantrasyon artışı ile pulmoner emboli ve astıma bağlı başvurular arasında güçlü ilişki mevcuttur.

**Anahtar sözcükler:** Hava kirliliği; acil servis başvuruları; iskemik inme; solunumsal ve kardiyovasküler hastalıklar.

## Introduction

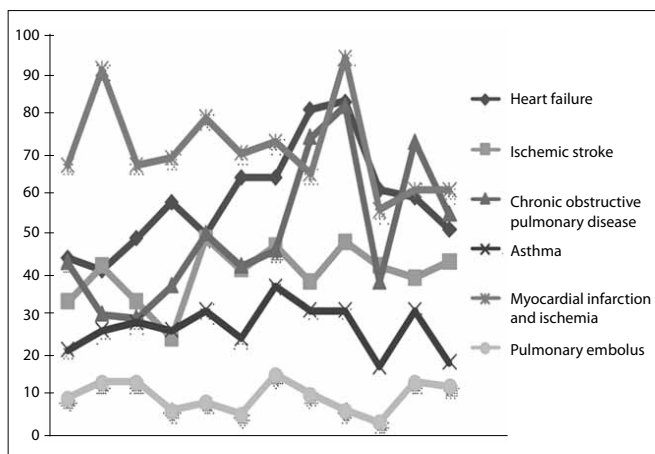
A recent some studies have shown that increased levels of air pollutants are positively associated with cardiovascular morbidity and mortality,<sup>[1,2]</sup> asthma,<sup>[3]</sup> ischemic stroke<sup>[4]</sup> and deep vein thrombosis.<sup>[5]</sup> Inhalation of air pollutants affects heart rate, heart rate variability, blood pressure, vascular tone, blood coagulability, and the progression of atherosclerosis. Although most studies focus on the influence of systemic effects, recent studies indicate that ultrafine particles may be translocated into the circulation and directly transported to the vasculature and heart where they can induce cardiac arrhythmias and decrease cardiac contractility and coronary flow.<sup>[6]</sup> Potential pathophysiological pathways include vascular dysfunction, inflammation, and oxidative stress and altered cardiac autonomic dysfunction.<sup>[7]</sup> The other effect is thrombosis. Hypercoagulability and enhanced thrombosis have been indicated as one mechanistic pathway that mediates such effects, since higher plasma levels of coagulation proteins such as factor VIII, von Willebrand factor, and fibrinogen have been associated with the exposure.<sup>[8]</sup> In animal models developed to investigate mechanisms involved in arterial thrombosis, inhalation or intravenous administration of air pollution constituents (such as diesel exhausts and ultrafine particles) induces thrombosis.<sup>[9,10]</sup> On the other hand, several studies reported associations between air pollution and pulmonary function. These include associations between short-term increases in levels of ambient particles smaller than 2.5 µm (PM<sub>2,5</sub>) or 10 µm (PM<sub>10</sub>) and increased hospitalizations,<sup>[8]</sup> increased asthma symptoms, and decreased pulmonary function.<sup>[11]</sup> The purpose of the present study was to determine the association between levels of ambient particulate air pollutants and Emergency Department (ED) visits for ischemic stroke, respiratory and cardiovascular disease in winter months, in the city of Izmir.

## Materials and Methods

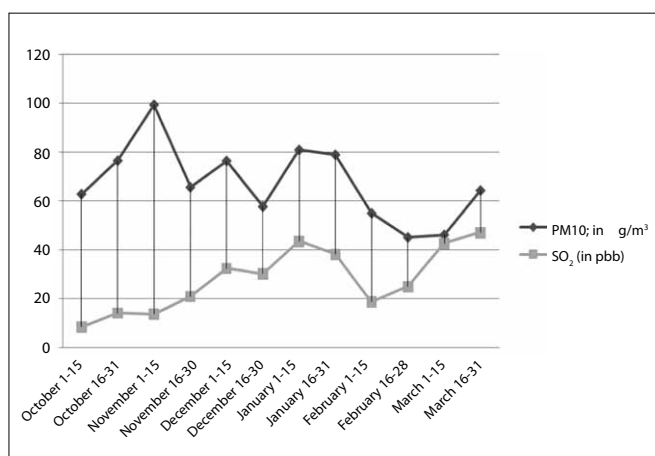
This cross sectional study was performed in a two university based emergency departments in Izmir (Ege University and Dokuz Eylul University Hospital) with an annual visit of approximately 60.000-70.000 patients for each hospital. We identified adult patients who had been presented to emergency department with cardiovascular and pulmonary diseases between October 1, 2008 and March 31, 2009. The ED visits were identified based on the discharge diagnosis and found to be as ischemic stroke (I63), transient ischemic attacks (G45), heart failure (I50), chronic obstructive pulmonary disease (J44), asthma (J45), acute myocardial infarction and ischemia (I20, I21, I22), using the International Classification for Diseases, (ICD-10). Visits in two weeks period were modeled and analyzed in a six month period from October 1, 2008 to March 31, 2009. Air pollution data were obtained from the National Air Quality Monitoring system archive. There were seven stations monitoring air pollution in Izmir during the study period. Daily mean and maximum pollution levels had been constructed from biweekly mean values for each site. For our study, we formed a period of bi-weekly average measurements to represent values of ambient particulate air pollution factors. Relations between carbon monoxide (CO), sulfur dioxide (SO<sub>2</sub>), and particulate matter (PM<sub>10</sub>), and visits for angina/myocardial infarction, heart failure, asthma, chronic obstructive pulmonary disease (COPD), and pulmonary embolus were examined. Data analysis was performed using the SPSS 14.0 for Windows software package (SPSS, Chicago, Ill). Associations between ambient particulate air pollution and ischemic stroke, respiratory and cardiovascular disease visits were investigated using statistical methods of multiple linear regression and bivariate correlation, Spearman's Rho test.

## Results

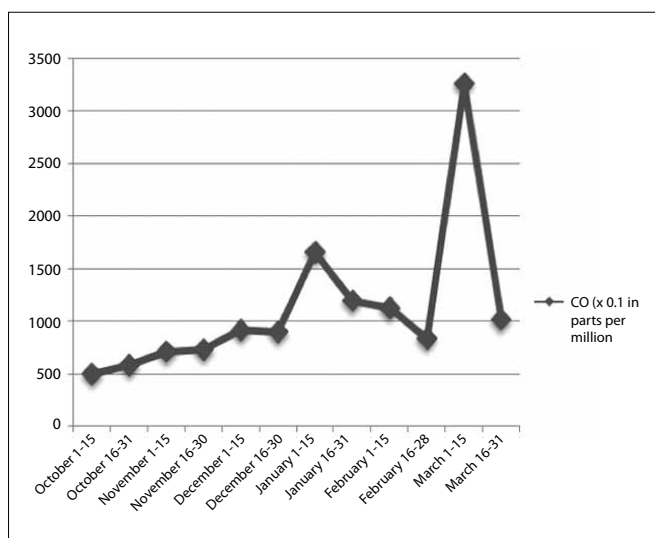
Total of 3070 ED visits including ischemic stroke, transient ischemic attacks, heart failure, chronic obstructive pulmonary disease, asthma, acute myocardial infarction and ischemia were included in the study within the 24 week period. Visits for myocardial infarction/angina exhibited the largest percentage of visits by adult patients with 27% (n=853), followed by heart failure with 23% (n=705), COPD with 20% (n=599), ischemic stroke with 16% (n=479), asthma with 10% (n=321) and pulmonary embolus with %4 (n=113). Total number of ED visits for



**Fig. 1.** Total number of ED visits for in each period of two weekly in six month.



**Fig. 2.** Distribution of air pollution concentrations in study period (PM10 and SO<sub>2</sub>).



**Fig. 3.** Distribution of average Carbonmonoxide measurements.

each period of two weeks during October 2008 - March 2009, are presented in Fig. 1. Trends of average PM10 and SO<sub>2</sub> levels by two-week periods is shown in Fig. 2 and carbon monoxide levels in Fig. 3. Average air pollution concentrations except in March were not widely deviated. The total number of ED visits each two-week period every month was compared with the average air pollution concentrations and are presented in Table 1. Significant bivariate correlations (rho spearman) were found among the COPD, MI and CO levels and asthma, pulmonary embolus and PM10 measurements respectively. Significant correlations were found between ED visits for asthma and the mean ambient concentrations of CO ( $p=0.024$ ,  $R^2=0.70$ ) measurements and PM10 ( $p=0.024$ ,  $R^2=0.70$ ). Statistically significant associations were observed between pulmonary embolus and PM10 ( $p=0.016$ ,  $R^2=0.55$ ) with multiple linear regression. And statistically significant associations were observed between angina/myocardial infarction and CO ( $p=0.001$ ) and SO<sub>2</sub> ( $p=0.005$ ) with bivariate correlation. We found no association between outdoor measures of CO, SO<sub>2</sub>, PM10 and heart failure, ischemic stroke and COPD visits.

## Discussion

A growing body of research supports the role of these air pollutants as aggravating acute and chronic diseases.<sup>[12]</sup> On a daily basis, humans inhale around 10,000 liters of ambient air, which comes in close contact with a lung surface area of over 100 m<sup>2</sup>. Rapid urbanization and industrialization with the concomitant increase in vehicular and industrial emissions, both in the developed and developing world, have significantly deteriorated the quality of air.<sup>[13]</sup> In most urban areas, traffic related emissions are a major source of air pollution. Truck, car, and bus traffic produces a complex mixture of toxic chemicals, PM, and a variety of irritant gases, including nitrogen dioxide, SO<sub>2</sub>, and O<sub>3</sub>. Children, the elderly, and persons with preexisting respiratory conditions, such as asthma, are among those most affected by air pollution.<sup>[14]</sup> Defined normal values of national primary air quality standards in the United States for carbon monoxide is 35 ppm, PM10 is 50 µg/m<sup>3</sup> and SO<sub>2</sub> 0.03 ppm.<sup>[15]</sup> The prevalence of bronchial asthma and the incidence of asthma exacerbation have been increasing in many countries. ED visits and hospital admission for asthma have also been increasing.<sup>[16]</sup> Evidence for association between air pollution from motor vehicles and asthma is still controversial. Among environmental fac-

**Table 1.** Bivariate correlation coefficient (*r*) between ED visits of cardiovascular and pulmonary disease and the various environmental.

	CO		PM10		SO <sub>2</sub>	
	r	p	r	p	r	p
Heart failure	0.245	0.443	-0.224	0.484	0.126	0.697
Ischemic stroke	-0.172	0.594	-0.137	0.672	0.182	0.571
Chronic obstructive pulmonary disease	0.580	0.48	-0.510	0.090	0.385	0.217
Asthma	0.070	0.829	0.664*	0.018*	-0.007	0.983
Myocardial infarction and ischemia	-0.818*	0.001*	0.259	0.417	-0.748*	0.005*
Pulmonary embolus	-0.084	0.795	0.686*	0.014*	0.028	0.931

p < .05 means significant.

tors, weather conditions and air pollution are suggested to play an important role in the increased trend for exacerbation of asthma for children<sup>[17]</sup> and adults.<sup>[18]</sup> Our results are consistent with some previous studies<sup>[18,19]</sup> that reported statistically significant relation between any of the air pollutants and adults ED visits for asthma.

Chronic obstructive pulmonary disease patients may suffer from recurrent disease exacerbations triggered by several factors, including air pollution. All particle fractions, accumulation, and coarse mode had especially adverse respiratory health effects among the elderly. Overall associations were stronger for respiratory than for cardiovascular outcomes.<sup>[20]</sup> We found a moderate relation between ED visits for COPD and particulate air pollution. There is still debate about how exacerbations should be defined and graded, and their mechanisms are poorly understood. The major causal agents are either bacteria or viral infections, or a combination of the them. Exacerbations represent an increase in the inflammation that is present in the stable state, with increased numbers of inflammatory cells, cytokines, chemokines and proteases in the airways, and increased concentrations of certain cytokines and C-reactive protein in the blood.<sup>[21]</sup> Particulates induce oxidative stress and, this leads to activation of histone acetylation and increased expression of interleukin-8. This is enhanced by adenoviral protein, suggesting that there may be an interaction between virus infection and air pollution in triggering exacerbations.<sup>[22]</sup> At the same time indoor air pollution from coal burning is an important risk factor for pneumonia death in adults.<sup>[23]</sup> Because of the high coal burning in winter months and ambient air pollution pattern in Izmir, chronic respiratory tract inflammation is thought to be additive effect of the high ED visits of COPD. Air pollution is associated with changes in the

global coagulation function, suggesting a tendency towards hypercoagulability after short-term exposure to air pollution. Few data on air pollution exposure and risk of venous thrombosis are available. Particulate air pollution has been consistently linked to increased risk of arterial cardiovascular disease and living near major traffic roads is associated with increased risk of deep vein thrombosis.<sup>[24]</sup> We found a positive association between ED visits for pulmonary embolus (PM10; p=0.016, R<sup>2</sup>=%55) and air pollution. Increased visits of pulmonary embolus and angina/myocardial infarction may relate to the ability of air pollution to increase plasma viscosity. Association for all cardiovascular mortality and morbidity with air pollution has been shown in several studies.<sup>[1,2]</sup>

There were some limitations in our study. First, this is a retrospective study performed in two centers with a relatively small number of visits. Multicenter studies produce more reliable and firm results. This study did not examine individual susceptibility to air pollution within the measure individual exposures. Occupational exposures, smoking and systemic diseases are among other contributory factors and they were not evaluated in our study. Further studies are needed to clarify the variable associations between particulate air pollution and relationship to both cardiovascular and respiratory disease and ischemic stroke.

**Conclusion**

In conclusion, no clinically significant associations were established between air pollutant concentrations and COPD, ischemic stroke and heart failure in adults. An increase in ambient levels of CO is associated with an increase in the number of ED visits for MI and asthma. PM 10 was strongly associated with pulmonary embolus and asthma visits during the warm season.

## Acknowledgment

The authors would like to thank to National Air Pollution Surveillance system of Turkey for providing current air pollution data.

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