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Particulate Matter ($PM_{2.5}$, $PM_{10\text{-}2.5}$, and PM_{10}) and Children's Hospital Admissions for Asthma and Respiratory Diseases: A Bidirectional Case-Crossover Study

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Epidemiological studies reported adverse effects of air pollution on the prevalence of respiratory diseases in children. The purpose of this study was to examine the association between air pollution and admissions for asthma and other respiratory diseases among children who were younger than 15 yr of age. The study used data on respiratory hospital admissions and air pollutant concentrations, including thoracic particulate matter (PM_{10}), fine ($PM_{2.5}$), and coarse ($PM_{10\text{-}2.5}$) particulate matter in Zonguldak, Turkey. A bidirectional case-crossover design was used to calculate odds ratios for the admissions adjusted for daily meteorological parameters. Significant increases were observed for hospital admissions in children for asthma, allergic rhinitis (AR), and upper (UPRD) and lower (LWRD) respiratory diseases. All fraction of PM in children showed significant positive associations with asthma admissions. The highest association noted was 18% rise in asthma admissions correlated with a 10-μg/m^3 increase in $PM_{10\text{-}2.5}$ on the same day of admissions. The adjusted odds ratios for exposure to $PM_{2.5}$ with an increment of 10 μg/m^3 were 1.15 and 1.21 for asthma and allergic rhinitis with asthma, respectively. PM_{10} exerted significant effects on hospital admissions for all outcomes, including asthma, AR, UPRD, and LWRD. Our study suggested a greater effect of fine and coarse PM on asthma hospital admissions compared with PM_{10} in children.

Experimental studies involving children health have shown that air pollutants, including ozone (O_3), sulfur dioxide (SO_2), inhalable particles, and nitrogen dioxide (NO_2), all aggravate airway pathology by inducing inflammation (Helander et al., 1997; Monn et al., 1999; Moshammer & Neuberger, 2003; Martonen & Schroeter, 2003; Yang et al., 2006). There is abundant evidence linking air pollution with respiratory symptoms, reduced lung function, childhood hospital admissions (Wilkinson et al., 1999; Nelson & Tony, 2000; Williams et al., 2000; Atkinson et al., 2001; Timonen et al., 2002), physician visits for upper and lower respiratory illness (Boezen et al., 1999), bronchitis and chronic cough (Chauhan & Johnston, 2003), asthma (Milligan et al., 1998), school absences (Park et al., 2002) and increased infant motility (Hauck et al., 2004).

However, emission, composition, and kinetics of aerosols are regionally different. Therefore, the investigation of typical local or regional situations is important in order to understand and interpret exposure data in combination with reliable analyses of adverse health effects. This is especially crucial for high-risk groups in order to establish the adverse health effects of PM exposure (Hauck et al., 2004).

The public is becoming more concerned about environmental issues, and at the same time new regulations are being enforced to control pollution deterioration of ambient air quality. Therefore, the analysis of the relationship between air pollution and health effects is gaining importance. For these reasons, this study focused specifically on children's respiratory health. When studying the health effects of exposure to hazardous agents, children are often considered as if they were small adults; however, children represent the largest subpopulation more susceptible than adults to the adverse health effects of air pollution (Mathieu-Nolf, 2002). Infants and children inhale and retain larger amounts of air pollutants per unit of body weight than adults and the air intake of a resting infant is twice that of an adult. In addition, their immature lungs may have a limited metabolic capacity to address these exposures (WHO, 2006). Children also spend more time outdoors than adults, and concentrations of pollutants of an ambient origin are higher outdoors than indoors.

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Zonguldak is the primary coal mining center of Turkey. A consequence of coal production was the increase in air quality degradation in Zonguldak. Underground mining directly impacts the health of those working underground, but also open-cast mining creates wider air quality deterioration due to dust and gaseous pollutants released in and around the mining complexes (Ghose & Majee, 2001). Zonguldak is the primary mining center of Turkey, with many underground coal mines, mainly run by the government. In fact, the local economy has relied heavily on coal mining and the coal industry for decades. At present, the coal mining industry, the electric power plant, the iron and steel factory, and the paper industry generate industrial air pollution in the city. The development of the city and rapid rise in the population were associated with the growth of this coal industry after the 19th century. Turkey's hard coal is mined only in the Zonguldak basin. A state-owned coal company, Turkish Hard Coal Enterprise (TTK), produces, processes, and distributes hard coal (1.5–2 million tons per year) from the Kozlu, Uzulmez, and Karadon coal mining sites. The coal produced is used mainly for power generation, in iron–steel plants, and for combustion. The coal produced is of poor quality and highly contaminating. An adverse consequence of rise in population and industrialization was the increase in environmental degradation, particularly in terms of air quality in Zonguldak. In Zonguldak, particulate matter (PM) containing hazardous heavy metals was emitted into the atmosphere unchecked, especially in the hard coal mining region. In Zonguldak, chronic respiratory asthma and chronic bronchial diseases are found to be prevalent. Epidemiological surveys showed that children and young adults suffer from asthma in this area (Tomaç et al., 2002). This study used the case-crossover method to examine the effects of PM exposure on daily counts of hospital admissions for children who were younger than 15 yr in Zonguldak, Turkey.

METHODS

Sampling Site

Zonguldak is a coastal city located in the western Black Sea region of Turkey at position 41°27′ N, 31°46′ E. It has a current population of approximately 110,000. The city is characterized by a "black diamond," signifying the importance attached to the coal produced in the area of the Kozlu, Uzulmez, and Karadon coal mining sites located 5 km west, 7 km souths and 12 km east of Zonguldak center, respectively (Figure 1).

The selection of the sampling site of air pollutant was based on the guidelines of the U.S. Environmental Protection Agency (U.S. EPA, 1997). The PM sampling station selection was made after a careful evaluation of the meteorological, topographical, land use characteristics in the study area, and

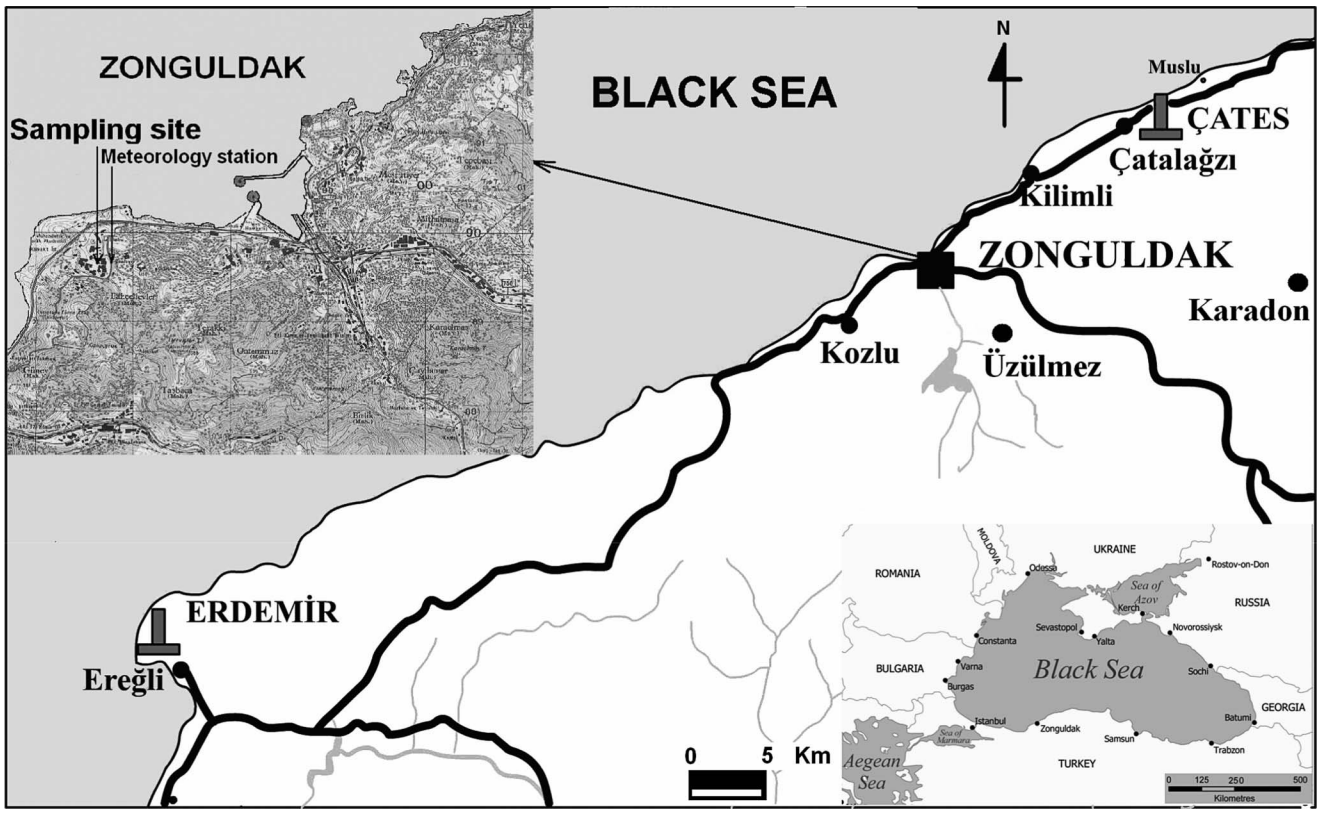

FIG. 1. Study area and sampling station

potential PM sources affecting the area. Accordingly, the selected sampling site fulfilled the aim of this study and represents the air quality of the surrounding area. Consequently, a dichotomous sampler was placed in the city center of Zonguldak city, particularly at the campus of Karaelmas University. The site is located approximately 4 m above sea level and has coordinates of 41.4508º N, 31.7726º E as seen in Figure 1. The site is not under the influence of any nearby direct source. Furthermore, the sampler is 100 m away from the nearest motorway. The collection of $PM_{2.5}$ and PM_{10} was performed using an Anderson automatic dichotomous sampler.

The Zonguldak area has a typical rainy and temperate Black Sea climate. However, as one moves away from the coastal area the weather becomes severe. The city is affected by marine and terrestrial winds of average 2.4 m/s. The dominant meteorological conditions are consistent with high pressure, high humidity, and foggy weather. During the study period, data for wind speed, temperature, vapor pressure, humidity, and cloudiness parameters were collected. Previous to this study period, meteorological observations were obtained form the nearby meteorology station operated by General Directorate of Meteorology.

Respiratory Health Data

This study was undertaken from December 2004 to October 2005, and data for daily hospital admission, PM, and meteorological information were collected. Respiratory admissions included the following conditions: asthma, allergic rhinitis, allergic rhinitis with asthma, and upper and lower respiratory diseases (9th revision of International Classification of Disease [ICD-9] 493, 470–478). Admissions for respiratory diseases in the sub-age group (0–14 yr) were selected as our study populations. The daily number of hospital admissions for respiratory diseases in children was determined by researchers from the Department of Pediatric Diseases, Faculty of Medicine (University of Karaelmas). Karaelmas University Practice and Research Hospital, established in Zonguldak, is a regional center for the Northwestern Black Sea region. Approximately, 115,000 patients are admitted and evaluated per year in all departments.

Statistical Analysis

Several study designs have been used to investigate the association between daily levels of air pollutants and consecutive acute changes in mortality and morbidity rates. The traditional air pollution time series studies such as APHEA in Europe or NMMAPS in the United States make up the vast majority of these investigations (Katsouyanni et al., 1997; Samet et al., 2000). However, the case-crossover design, first described in 1991 (Maclure, 1991), offers an alternative approach to investigate acute effects (Navidi & Weinhand, 2002). The case-crossover design compares ambient air pollutant concentrations at an event with concentrations on a control day. The case-crossover approach also permits the use of individual characteristics such as age, gender, health status, or lifestyle factors to assess effects of air pollution among potentially susceptible subgroups or to explore modification of air pollutant effects by individual characteristics (Jaakkola, 2003; Bateson, 2004). In the case-crossover design, the study population consists of subjects or cases that have experienced an episode of the health outcome of interest. The design focuses on the point in time when the event occurred (Jaakkola, 2003). In the traditional air pollution time-series studies, the relevant exposure term is the daily level of some ambient air pollutant concentrations at or shortly before an event with concentrations on a control day. Under the null hypothesis, “exposure” on control days should not be different from “exposure” at (or shortly before) the event. If ambient air pollution has a true effect on the event probability, the null hypothesis can only be rejected if the nature of the ambient air pollution time series is such that the difference between event and control days shows sufficient variation around a nonzero mean value. Control days are selected in various ways, most often 7, 14, or 21 d before and/or after the event to control for time-varying cofactors that might be associated with day of the week (Künzli & Schindler, 2005). Simulation studies showed that bidirectional control periods (7, 14, or 21 d before and after the event day) result in less bias (Janes et al., 2004; Sunyer et al., 2002; Tsai et al., 2003). This design controls for bias due to time trend and confounding by both season and day of the week if referents are within the same season and on the same day of the week as the index time (Bateson & Schwartz, 1999; Sunyer et al., 2002; Tsai et al., 2003). In this analysis, a symmetric bidirectional case-crossover approach was used. The level of PM at the time of admission for each case (the case period) was compared with a level obtained in a specified period before and after the health event (the control period). Control days are the same day of the week as the case days. Cases in this analysis included only children in the study area with respiratory diseases during the study period. Using covariates, there were additional controls as follows: winter, spring, summer, and autumn temperature, cloudiness, pressure, wind speed, and maximum wind speed. The acute effects of air pollution exposure may be immediate or may occur several days after exposure. Several studies reported that increased admissions are strongly associated with air pollution on the day of admission or within up to 4 d (Norris et al., 1999; Burnett et al., 1999). In this study, the lag up to 4 previous days was used to examine the effect of lag days of PM ending on the admission day.

The case-crossover study design offers the ability to control confounders by design rather than by modeling. This design is an adaptation of the case-control study in which each case serves as his or her own referent. Therefore, time-invariant subject-specific variables such as gender and age do not act as confounders (Tsai et al., 2003). Control periods of 2 wk before and after the admission date were used in this analysis. By selecting 2 wk before and 2 wk after the date of respiratory admission as the control, this approach avoids possible

confounding resulting from the effects of day of the week, seasonality, or chronic trends. This study applied conditional logistic regression models for the case-crossover design by using the Stata statistical package's clogit procedure (Stata Corp, 2005). Conditional logistic regression analysis was used to estimate adjusted odds ratios (ORs). This analysis allows modeling using several or a varying number of control periods. Exposure may be characterized quantitatively using the level, cumulative exposure, exposure time, exposure profile, or a meaningful combination of these. ORs were calculated for PM with respect to asthma and other respiratory admissions after adjusting for weather conditions including daily temperature, average relative humidity, pressure, cloudiness, and average and maximum wind speed. Results of previous studies indicated that increased mortality or hospital admissions were associated with high air pollution levels on the same day or the previous days (Norris et al., 1999; Burnett et al., 1999). Thus, the cumulative lag up to 4 previous days was used. The associations between hospital admissions and levels of air pollutants were estimated by use of ORs and their 95% confidence intervals (CIs), which were produced through conditional logistic regression with weights equal to the number of admissions on that day. The ORs were calculated on the basis of an increment in exposure corresponding to the 10-mg/m^3 and interquartile range (IQR; differences between the 25th and 75th percentiles) of $PM_{2.5}$, $PM_{10\text{-}2.5}$, and PM_{10}.

RESULTS

During the study period, there was a total of 2779 hospitalizations for respiratory diseases in children who were 0 to 14 yr of age with a daily average of 14 children/d in Zonguldak. Admission for respiratory diseases were categorized as asthma, allergic rhinitis with asthma (AR with Asthma), allergic rhinitis (AR), upper respiratory disease (UPRD), and lower respiratory disease (LWRD). Table 1 provides a summary for hospital admissions for respiratory diseases, air pollution, and weather conditions. Results of admission of respiratory symptoms in Zonguldak showed a higher prevalence for asthma and allergies among the symptoms/diseases.

The average mass concentration of fine ($PM_{2.5}$) and coarse ($PM_{2.5\text{-}10}$) PM during the study period was 29.1 μg/m^3 and 24.3 μg/m^3, respectively. PM mass concentrations are given in Table 1. The annual average value for PM_{10} was 53.3 μg/m^3, which is less than the U.S. EPA annual average limit of 60 μg/m^3. The U.S. EPA annual average limit for $PM_{2.5}$ is 15μg/m^3, while the measured $PM_{2.5}$ value at Zonguldak city was 29.1μg/m^3, which is approximately twice the U.S. EPA limit value. As

TABLE 1
Summary statistics for hospital admissions, air pollutants and weather data

					Percentiles			
Variable	Days	Mean	Median	Sum	Min	25th	50th	75th	Max
Hospital admissions, n									
Asthma	94	1,99	1	187	0	1	1	2	12
AR with asthma	150	3,09	3	463	1	2	3	4	9
Allergic Rhinitis	152	2,79	2	424	1	1	2	4	9
Upper RD	35	1,54	1	54	1	1	1	2	5
Lower RD	36	3,17	2	114	1	1	2	5	10
Air pollutants (μg/m^3)									
$PM_{2.5}$	293	29,1	26,08		4,55	20,83	26,09	34,78	95,65
$PM_{10\text{-}2.5}$	293	24,3	20,83		4	13,61	20,83	27,27	195,8
PM_{10}	293	53,3	45,8		12	35,8	45,8	62,5	237,5
$PM_{2.5}/PM_{10\text{-}2.5}$	293	1,49	1,25		0,21	0,99	1,252	1,87	7,53
$PM_{2.5}/PM_{10}$	293	0,56	0,55		0,17	0,499	0,55	0,65	0,88
Weather conditios									
RH, %	293	74,4	78		29	68,3	78	83,5	95
Winter_temp, °C	70	7,24	7		–0,1	4,47	7	9,55	17,4
Spring_temp, °C	92	11,3	12,2		0,8	6,3	12,2	16,47	23,5
aut_temp, °C	92	21,8	22,55		15,9	20,05	22,55	23,6	26,8
Summer_temp, °C	39	18,9	19,1		14,9	17,4	19,1	20,8	22,6
Pressure, mb	293	13,6	13,3		4,1	8	13,3	19,25	26,2
Cloud, x/10	293	4,76	4,7		0	1,7	4,7	8	10
Wind speed, m/sec	293	2,21	2		0,3	1,4	2	2,9	6,8
max_wind, m/sec	293	8,46	7,5		1,6	5,45	7,5	10,6	22,8

seen in Table 1, mean and median values for the ratio of $PM_{2.5}/PM_{10}$ were 0.56 and 0.55, respectively, and the 75th percentile value was 0.65. Throughout the year, the $PM_{2.5}$ mass concentration in each season was higher than $PM_{2.5\text{-}10}$. As a result, the mass concentration of $PM_{2.5}$ particle size is predominant. Compared to many European cities this concentration is one of the highest (Begum et al., 2004; Gomiscek et al., 2004; Querol et al., 2004). During the entire study the two particle sizes $PM_{2.5}$ and $PM_{10\text{-}2.5}$ showed a significant correlation. The mean $PM_{2.5}/PM_{10\text{-}2.5}$ ratio was 1.49 with a median ratio of 1.25.

Air Pollution Levels and Admission for Respiratory Diseases

The results obtained using the case-crossover design with different lag times were subjected to logistic regression analyses with adjustment on meteorological variables. Table 2 provides adjusted ORs and their 95% CIs for exposures to each air pollutant in relation to admissions for respiratory diseases separately. Pollutant exposures used were the average of the current and previous 4 d. Estimates of percent increase in morbidity are shown for 10 $\mu g/m^3$ and interquartile range rise. These interquartile ranges for 24 h were as follows: 13.95 $\mu g/m^3$ $PM_{2.5}$, 13.67 mg/m^3 $PM_{10\text{-}2.5}$, 26.70 mg/m^3 PM_{10}. Table 2 shows an association between an elevation in short-term air pollution levels and respiratory hospital admissions for PM. For all PM fractions ($PM_{2.5}$, $PM_{10\text{-}2.5}$, and PM_{10}) there were consistent significant positive associations with hospital admission for asthma (Table 2). The adjusted OR for lag0 and lag4 exposure to $PM_{2.5}$ with an increment of 10 mg/m^3 was 1.15 and 1.25, respectively. For an interquartile (13.95 $\mu g/m^3$) increase, the adjusted OR was 1.22 and 1.37. The corresponding OR for $PM_{10\text{-}2.5}$ on the day of admission (lag0) and at lag4 with an increment of 10 $\mu g/m^3$ was 1.18 and 1.17, respectively. For an interquartile (13.67 $\mu g/m^3$) rise, adjusted OR was 1.26 and 1.24. The adjusted ORs for lag0 and lag4 exposure to PM10 with an increment of 10 $\mu g/m^3$ and interquartile (26.70 $\mu g/m^3$) were 1.14, 1.16 and 1.42, 1.47, respectively. Among the same-day to 4-d lags of air pollutant exposure, the same day and 4-d lag PM levels were found to have the strongest effects on asthma diseases after controlling for meteorological variables and time-dependent confounders.

In this case-crossover, the same-day $PM_{10\text{-}2.5}$ showed a stronger effect on asthma admission than did $PM_{2.5}$ and PM_{10}. However, the 4-d lag $PM_{2.5}$ level demonstrated the strongest effects on asthma admissions. For an increase of 10 $\mu g/m^3$ and IQR on the previous 4 d, the elevation in the number of admissions was equal to 25 and 37%, respectively. In addition, there was a statistically significant association between ARwithAsthma admission and $PM_{2.5}$ levels on the day of admission. For an increase of 10 mg/m^3 on the same day, the rise in admission was 21%. For the same elevation for PM_{10}, the increase in the risk was 7%. The OR for lag2 exposure to $PM_{10\text{-}2.5}$ with an increment of 10 $\mu g/m^3$ was 1.08. Data showed that $PM_{2.5}$ was the strongest predictor for allergic rhinitis with asthma (ARwithAsthma) admissions. There was a statistically significant association between allergic rhinitis (AR) and all fractions of PM. The lag2 $PM_{10\text{-}2.5}$ demonstrated a stronger effect on the AR admission than did $PM_{2.5}$ and PM_{10}. The estimated ORs for $PM_{10\text{-}2.5}$, $PM_{2.5}$, and PM_{10} corresponding to an increase of 10 $\mu g/m^3$ with the previous 4 d were 1.15, 1.18, and 1.09, respectively. The results for asthma, ARwithAsthma, and AR showed the $PM_{2.5}$ fraction to be a more reliable predictor of asthma admissions than $PM_{10\text{-}2.5}$ and PM_{10} fractions in children. However, the effect of $PM_{10\text{-}2.5}$ on asthma admissions found in our study was nearly equal to that of the $PM_{2.5}$ fraction. This may be a result of the fact that the mass concentration of $PM_{2.5}$ particle size is predominant.

DISCUSSION

Throughout the study period, the $PM_{2.5}$ mass concentration in each season is higher than $PM_{10\text{-}2.5}$. Studies suggest that pollutants enhance allergic sensitization in those genetically at risk, lending plausibility to the role of potentially injurious effects of ambient air pollutants in the causation of pediatric lung disease, including asthma (Wilkinson et al., 1999; Milligan et al., 1998; Nelson & Tony, 2000; Williams et al., 2000; Atkinson et al., 2001; Timonen et al., 2002; Boezen et al., 1999). Although the relationship between $PM_{10\text{-}2.5}$ and asthma hospitalization has not been well documented, $PM_{10\text{-}2.5}$ showed stronger positive effects on other health outcomes such as mortality from all causes, respiratory diseases, and cardiovascular disease, as well as hospitalizations for cardiovascular diseases (Loomis, 2000). It is not known whether respiratory effects of $PM_{2.5}$ are greater than those of $PM_{10\text{-}2.5}$. In a study at Toronto (Burnett et al., 1999) found the $PM_{10\text{-}2.5}$ fraction to be a more reliable predictor of asthma admissions than the $PM_{2.5}$ and PM_{10} fractions in subjects of all ages. The estimated relative risks for $PM_{10\text{-}2.5}$, $PM_{2.5}$, and PM_{10} corresponding to an increase of 10 $\mu g/m^3$ with 3-d averaging were 1.04, 1.01, and 1.01, respectively. Although there is no clear explanation for such a discrepancy regarding the influences of PM_{10} and $PM_{2.5}$ on asthma hospitalizations, reasons may include variability in population characteristics, natural systems, and the complex mixture of fine particles with a different level and composition over time and space.

There was no significant association between $PM_{2.5}$ and hospital admission for UPRD and LWRD in children. A statistically significant effect for $PM_{10\text{-}2.5}$ and PM_{10} was found for UPRD and LWRD. A 10-$\mu g/m^3$ change in PM_{10} was associated with a risk of 1.15 and 1.23, respectively, for upper and lower respiratory diseases. Coarse $PM_{10\text{-}2.5}$ and PM_{10} in this study were related to hospital admission, with a lag of about 4 d, but $PM_{2.5}$ was not a better predictor of hospital admission for UPRD and LWRD. There have been several studies of ambient PM_{10} exposure and risk for upper and lower respiratory

TABLE 2

Adjusted odds ratio (OR) with 95% confidence intervals for hospital admissions for respiratory diseases

Hospital Admissions	10 µg/m^3 increase						IQR range increase					
	$PM_{2.5}$		$PM_{10-2.5}$		PM_{10}		$PM_{2.5}$		$PM_{10-2.5}$		PM_{10}	
	OR	CI (95%)	OR	CI (95%)	OR	CI (95%)	OR	CI (95%)	OR	CI (95%)	OR	CI (95%)
Asthma												
Lag 0	1,15*	0,99–1,34	1,18*	1,01–1,39	1,14*	1,03–1,26	1,22**	0,99–1,51	1,26*	1,01–1,57	1,42*	1,09–1,84
Lag 1	0,85	0,70–1,03	0,92	0,78–1,08	0,92	0,83–1,02	0,79	0,61–1,04	0,89	0,71–1,11	0,80	0,61–1,05
Lag 2	0,87	0,73–1,04	0,98	0,84–1,15	0,92	0,81–1,03	0,83	0,65–1,06	0,97	0,78–1,20	0,79	0,58–1,08
Lag 3	0,93	0,79–1,10	1,11	0,97–1,27	1,01	0,92–1,11	0,90	0,72–1,14	1,16	0,96–1,39	1,02	0,80–1,31
Lag 4	1,25*	1,05–1,50	1,17*	1,05–1,31	1,16*	1,06–1,26	1,37**	1,06–1,76	1,24*	1,07–1,44	1,47*	1,17–1,86
ARwithasthma												
Lag 0	1,21*	1,10–1,33	0,96	0,88–1,04	1,07*	1,01–1,13	1,31*	1,15–1,49	0,94	0,84–1,05	1,19*	1,02–1,38
Lag 1	0,84	0,75–0,93	1,08*	0,99–1,18	0,96	0,91–1,02	0,78	0,67–0,90	1,11*	0,99–1,25	0,91	0,77–1,06
Lag 2	0,89	0,81–0,98	0,93	0,86–1,02	0,93*	0,88–0,99	0,85	0,74–0,98	0,91	0,81–1,02	0,83*	0,71–0,98
Lag 3	0,99	0,90–1,09	0,94	0,86–1,03	0,96	0,90–1,02	0,99	0,86–1,13	0,92	0,81–1,05	0,90	0,76–1,06
Lag 4	1,06	0,95–1,19	1,10*	1,03–1,18	1,08*	1,02–1,14	1,09	0,93–1,27	1,14*	1,04–1,26	1,23*	1,06–1,42
AllergicRhinitis												
Lag 0	1,08	0,98-1,20	1,06	0,95–1,19	1,06	0,99–1,13	1,11	0,97–1,28	1,09	0,94–1,27	1,16	0,97–1,40
Lag 1	1,03	0,93–1,13	1,17*	1,04–1,31	1,08*	1,01–1,16	1,04	0,91–1,19	1,23*	1,06–1,44	1,24*	1,04–1,48
Lag 2	0,89	0,80–0,99	0,92	0,84–1,02	0,92*	0,87–0,99	0,85	0,73–0,98	0,90	0,79–1,02	0,81*	0,68–0,97
Lag 3	0,98	0,89–1,09	0,99	0,91–1,08	0,97	0,92–1,03	0,98	0,85–1,12	0,98	0,88–1,11	0,93	0,80–1,09
Lag 4	1,18*	1,00–1,24	1,15*	1,06–1,25	1,09*	1,03–1,16	1,16*	0,99–1,35	1,22*	1,09–1,36	1,27*	1,09–1,48
Upper RD												
Lag 0	0,99	0,49–2,00	0,80	0,54–1,19	0,88	0,68–1,14	0,98	0,37–2,63	0,74	0,43–1,26	0,72	0,36–1,41
Lag 1	0,52	0,22–1,20	1,22	0,92–1,61	1,17	0,91–1,51	0,40	0,12–1,29	1,31	0,90–1,91	1,52	0,78–2,98
Lag 2	1,29	0,75–2,22	0,97	0,70–1,33	1,00	0,76–1,31	1,43	0,67–3,03	0,95	0,62–1,47	1,00	0,48–2,07
Lag 3	1,29	0,69–2,43	0,94	0,66–1,33	0,95	0,76–1,19	1,43	0,59–3,44	0,92	0,57–1,47	0,87	0,48–1,58
Lag 4	1,47	0,87–2,50	1,08	0,88–1,32	1,15*	0,97–1,35	1,71	0,82–3,58	1,11	0,84–1,46	1,44*	0,93–2,24
Lower RD												
Lag 0	1,06	0,78–1,44	0,90	0,71–1,16	1,01	0,86–1,19	1,08	0,70–1,66	0,87	0,62–1,22	1,03	0,67–1,58
Lag 1	0,85	0,59–1,22	1,20*	0,97–1,50	1,04	0,88–1,23	0,79	0,48–1,32	1,29*	0,95–1,74	1,11	0,72–1,74
Lag 2	1,08	0,72–1,61	1,00	0,84–1,19	1,04	0,92–1,18	1,11	0,64–1,94	1,00	0,78–1,28	1,11	0,80–1,55
Lag 3	1,18	0,92–1,52	1,26*	1,08–1,47	1,23*	1,07–1,41	1,27	0,89–1,80	1,37*	1,12–1,69	1,73*	1,19–2,50
Lag 4	0,72	0,54–0,96	1,02	0,93–1,13	0,99	0,90–1,08	0,64	0,43–0,95	1,03	0,90–1,18	0,97	0,76–1,24

The OR were calculated for a 10 µg/m^3 and interquartile range increment of particulate matter (and subfractions); adjusted ORs were adjusted for daily weather conditions.

*p ≤ .05

**p ≤ .01

diseases in children. A study in Thailand (Vichit-Vadakan et al., 2001) investigated daily upper and lower respiratory symptoms in 3 categories consisting of children, adults, and nurses in relation to daily outdoor $PM_{2.5}$ and PM_{10} concentrations over 3 mo. A 45-$\mu g/m^3$ (approximately interquartile range) change in PM_{10} was associated with risk of 1.10 and 1.13, respectively, for UPRD and LWRD in children. One study reported a 3.7 and 5.1% increase in upper and lower respiratory symptoms, respectively, per 10-$\mu g/m^3$ increase in PM_{10} (Pope et al., 1991). Anderson et al. (2001) evaluated a range of air pollutant measures in relation to hospital admissions in the West Midlands in the United Kingdom during the period 1994–1996. Separate measures for fine ($PM_{2.5}$) and coarse ($PM_{10-2.5}$) particles were available in this study, together with PM_{10}, black smog, SO_2, and O_3. A significant effect for PM_{10} and black smog (and SO_2) was found, but neither $PM_{2.5}$ nor $PM_{10\text{-}2.5}$ was a better predictor of hospital admissions for asthma than PM_{10}.

A bidirectional case-crossover design was used in this study. The case-crossover design and conditional analysis used in this study controlled for seasonality, time trends, and weekday (and any interaction between them) by design, thereby eliminating any residual confounding. The case-crossover design used has several advantages over the classical ecological pattern. First, all patients' characteristics and environmental influences other than short-term meteorological changes are eliminated because the patient serves as his (her) own control. Further, by choosing 2 wk prior to and 2 wk after the date of hospital admission as the controls, this approach might avoid possible confounding resulting from the effects of day of the week, seasonality, or long-term trends. This study found significant, consistent associations between children's hospital admissions and outdoor air pollutants in the urban center of Zonguldak for PM and subfractions.

There was evidence of positive associations between day-to-day variation in $PM_{2.5}$ concentration and hospital admissions for all outcomes, except UPRD and LWRD, for 1 exposure, lag0 and lag4. The highest effect was found at lag 4 for asthma admissions. This survey demonstrated a 15 and 25% increase in the hospital admissions for asthma in relation to a rise of 10 mg/m^3 in $PM_{2.5}$ levels, the same day and 4 d prior. In addition, there was a significant association between allergic rhinitis with asthma (ARwithAsthma) admissions and $PM_{2.5}$ level on the day of admission, with an estimated increase of 21% per 10-mg/m^3 rise in $PM_{2.5}$ (Table 2).

Although many time-series studies used PM_{10} as an exposure indicator, only a few studies specifically assessed associations of $PM_{2.5}$ with hospitalization or other morbidity measures (U.S. EPA, 2005). Lippmann et al. (2000) and Ito et al. (2005) used Medicare admission data for Detroit, MI, for 1992–1994, along with size-fractionated PM concentration data in Windsor, Ontario. Updated analyses of these data showed positive associations of $PM_{2.5}$ for hospitalization for pneumonia, chronic obstructive pulmonary disease (COPD), ischemic heart disease, and heart failure. Several studies reported that $PM_{2.5}$ was significantly associated with risk for hospital admission for cardiovascular disease and hospital admission for asthma (Moolgavkar, 2000a, 2000b; Sheppard, 2003). An estimated 4 to 5% increase in the rate of asthma hospital admissions (lagged 1 d) was reported to be associated with interquartile range changes in $PM_{2.5}$ (11.8 $\mu g/m^3$), equivalent to an excess risk rate of 9% per 25 $\mu g/m^3$ $PM_{2.5}$. In addition, Norris et al., (1999) showed associations of low levels of PM2.5 (mean = 12 $\mu g/m^3$) with markedly elevated asthma excess risk (ED) 44.5% or 4 admissions per 25 $\mu g/m^3$ $PM_{2.5}$.

Although PM_{10} mass has most often been implicated as the PM pollution index affecting respiratory hospital admissions, the new studies appear to suggest relative roles for PM_{10} and for both fine and coarse thoracic PM mass fractions, such as $PM_{2.5}$ and $PM_{10\text{-}2.5}$. $PM_{10\text{-}2.5}$ tended to exert a greater effect on hospitalization for respiratory diseases than $PM_{2.5}$, which is consistent with previous findings for asthma hospitalizations in children (Dominici et al., 2005, 2006; Lin et al., 2002, 2005). Lin et al. (2002) used both case-crossover and time-series analyses to assess the associations between size-fractionated PM and asthma hospitalization in children 6–12 yr old living in Toronto between 1981 and 1993. Time-series plots of the $PM_{2.5\text{-}10}$ data showed stronger seasonality effects in the estimated coarse PM data than in the estimated fine PM mass data. Using a bidirectional case-crossover analysis, the estimated relative risks (RR) were 1.14 for males and 1.18 for females, for an increment of 8.4 $\mu g/m^3$ in 6-d averages of $PM_{10\text{-}2.5}$. Several new U.S. and Canadian studies yielded particularly interesting results that are also suggestive of roles for both fine and coarse particles in respiratory-related hospital admissions. Lippmann et al. (2000) and Ito et al. (2005) found comparable effect size estimates for $PM_{2.5}$ and $PM_{10\text{-}2.5}$. That is, the excess risk for pneumonia hospital admissions (in no copollutant model) was 18.6% per 50 $\mu g/m^3$ PM_{10}, 10% per 25 $\mu g/m^3$ $PM_{2.5}$, and 11.2% per 25 $\mu g/m^3$ $PM_{10\text{-}2.5}$. Sheppard et al. (1999) and Sheppard (2003) studied relationships between PM metrics that included $PM_{10-2.5}$ and nonelderly adult hospital admissions for asthma in the greater Seattle area and reported significant RR for PM_{10}, $PM_{2.5}$, and $PM_{10\text{-}2.5}$ (lagged 1 d). For $PM_{10\text{-}2.5}$, RR was 1.05; for $PM_{2.5}$, RR was 1.07. The effect of $PM_{10\text{-}2.5}$ on asthma admissions found in our study was greater than the effect of $PM_{2.5}$ on the same day of admission, but lower with a lag of 4 d. Evidence suggests that $PM_{10\text{-}2.5}$ and $PM_{2.5}$ exert similar effects on asthma hospital admissions. Finally, significant positive associations were found between PM_{10} concentration and hospital admissions for all outcomes. For an increase of 10 $\mu g/m^3$ in PM_{10} on the same day and 4 d prior (lag4), the elevation of asthma admissions were equal to 14 and 16%, respectively. The effect of PM_{10} on asthma admissions was found to be lower than for $PM_{2.5}$ and $PM_{10\text{-}2.5}$.

There are numerous studies on PM_{10} and risk for hospitalization, which generally show positive associations (Krewski et al., 2005; Dominici et al., 2005). In a study by

Sheppard et al. (1999) that evaluated relationships between measured ambient pollutants and nonelderly adult (<65 yr of age) hospital admissions for asthma in Seattle, PM and CO were found to be jointly associated with asthma admissions with equivalent to ED 13% per 50 $\mu g/m^3$ for PM_{10}. Nauerberg and Basu (1999) also reported PM_{10} associations with asthma hospital admissions of an increase of 16.2% per 25 $\mu g/m^3$ in PM_{10}. Several studies included $PM_{2.5}$ and PM_{10} independently in their analyses of peak flow. Of these, Pekkanen et al. (1997) and Romieu et al. (1996) found comparable results for $PM_{2.5}$ and PM_{10}, while Peters et al. (1997) reported larger effects for $PM_{2.5}$. Of studies that included both PM_{10} and $PM_{2.5}$ in their analyses of respiratory symptoms, Peters et al. (1997) found similar effects for the two PM measures. Only the Romieu et al. (1996) study showed greater effects for $PM_{2.5}$. There are no clear explanations for such a discrepancy regarding the influences of PM_{10} and $PM_{2.5}$ on asthma hospitalizations. Differences may be due to variability in population characteristics, natural systems, and the complex mixture of fine particles with a different level and composition over time and space. While the PM associations with adverse health effects among asthmatics and others are well documented, the type/sources of PM most associated with adverse health effects among asthmatics are not known at this time. Indeed, the makeup of PM varies greatly from place to place and over time, depending upon factors such as the sources that contribute to pollution and the prevailing atmospheric conditions, affecting particle formation, coagulation, transformation, and transport. In summary, a stronger positive effect of $PM_{10\text{-}2.5}$ and $PM_{2.5}$ was found on asthma admissions compared with PM_{10} for children, using both bidirectional case-crossover analyses.

A significant effect for PM_{10} was found for AR, UPRD, and LWRD on several exposure lag days. Estimated increases in AR admissions on lag 1 and lag 4 were 8 and 9%, respectively. An elevation of 15% in the hospital admissions of UPRD was estimated for each 10-$\mu g/m^3$ increase in PM10 and a 23% rise in hospital admissions of LWRD for each 10-$\mu g/m^3$ increase in PM_{10}. Among the PM fractions, PM_{10} is the only pollutant to exert effects on UPRD admissions. Dockery and Pope (1994) analyzed the combined epidemiological studies data of children and estimated a mean increase of 3% and 0.7% in the prevalence of LWRD and UPRD for an elevation of 10 $\mu g/m^3$ in PM_{10}, respectively. The other study reported a 3.7 and 5.1% increase in UPRD and LWRD, respectively, per 10-$\mu g/m^3$ rise in PM_{10} (Pope et al., 1991). In conclusion, this bidirectional case-crossover design study demonstrated significant associations between children's hospital admissions for asthma and respiratory outcomes and outdoor PM in the urban area center of Zonguldak for all fractions of PM.

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