BMC Public Health

RESEARCH

Open Access

Association between air pollutants and blood cell counts in pediatric patients with asthma: a retrospective observational study

Kuo-Chen Huang[1], Hsiu-Yung Pan[1], Ting-Min Hsieh[2], Chih-Cheng Chen[3] and Fu-Jen Cheng[1,4*]

Abstract

Background Asthma is a common respiratory disease in children, and air pollution is a risk factor for pediatric asthma. However, how air pollution affects blood cells in pediatric patients with asthma remains unclear.

Methods This retrospective observational study, performed in 2007–2018 at a medical center, enrolled non-trauma patients aged < 17 years who visited the emergency department and had asthma. Medical records and blood cell counts, including absolute neutrophil count (ANC), eosinophil count, and platelet count were extracted. The concentrations of $PM_{2.5}$, PM_{10}, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) were measured from 11 air-monitoring stations in Kaohsiung City.

Results One-unit increases in $PM_{2.5}$ (regression coefficient: 25.618; S.E.: 5.937; $p < 0.001$), PM_{10} (19.97; 3.541; $p < 0.001$), NO2 (70.681; 15.857; $p < 0.001$), SO_2 (81.694; 30.339; $p = 0.007$), and O_3 (23.42; 8.831; $p = 0.022$) on lag 0–6 (7 d average) correlated positively with ANC. One-unit increases in $PM_{2.5}$ (0.859; 0.357; $p = 0.016$), PM_{10} (0.728; 0.213; $p = 0.001$), and SO_2 (4.086; 1.811; $p = 0.024$) on lag 0–6 correlated positively with eosinophil count. Additionally, one-unit increases in $PM_{2.5}$ (0.302; 0.101; $p = 0.003$) and PM_{10} (0.229; 0.06; $p < 0.001$) on lag 0–6 correlated positively with platelet count. In a two-pollutant model, the impacts of $PM_{2.5}$ and PM_C on ANC and platelet count remained statistically significant after adjusting for other air pollutants. Additionally, PM_C correlated significantly with eosinophil count after adjusting for $PM_{2.5}$, NO_2, SO_2, and O_3. Quartile increases in $PM_{2.5}$ and PM_C levels correlated positively with ANC, eosinophil count, and platelet count (all p for trend < 0.05).

Conclusions $PM_{2.5}$, PM_C, and NO_2 were independently and positively associated with ANC, PM_C was positively associated with eosinophil count, and $PM_{2.5}$ and PM_C were positively associated with platelet count in pediatric patients with asthma. Our results highlight the relationship between air pollution and blood cell counts in pediatric patients with asthma.

Keywords Air pollutant, Blood cell counts, Pediatric, Asthma, Particulate matter

*Correspondence:
Fu-Jen Cheng
a0953283092@yahoo.com.tw
[1]Department of Emergency Medicine, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, No. 123, Dapi Road, Niaosong Township, Kaohsiung County 833, Kaohsiung City, Taiwan
[2]Division of Trauma, Department of Surgery, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung City, Taiwan
[3]Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung City, Taiwan
[4]Institute for Translational Research in Biomedicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan

Background

Numerous studies have indicated that short-term variations in air pollution can have adverse health effects such as cause respiratory and cardiovascular diseases and increase daily mortality [1–4]. Fine particulate matter, defined as particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$), is currently considered to pose a greater health risk than larger particles [5, 6]. These health effects may vary seasonally and regionally. Multiple city-level studies have shown that the health effects associated with PM differ regionally [7, 8]. One possible reason for this is that the composition of $PM_{2.5}$ and the concentrations of other air pollutants, such as nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3), change regionally and seasonally. For example, the concentrations of certain heavy metals in $PM_{2.5}$ from anthropogenic sources, such as cadmium, lead, antimony, and selenium, are higher in Ningbo, China, in winter [9]. In industrial areas, the concentrations of NO_2 and SO_2 are high, while the concentration of O_3 is related to photochemical reactions. The health risks associated with $PM_{2.5}$ vary owing to differences in their composition and interactions with other air pollutants [10].

Respiratory diseases are common causes of mortality in children, resulting in 1.3 million deaths in children under five years of age between 2010 and 2011 [11]. The components of air pollution, such as particulate matter (particulate matter with an aerodynamic diameter of < 10 μm, PM_{10}), $PM_{2.5}$, NO_2, and O_3, are associated with respiratory inflammation [12]. Epidemiological studies have also found that $PM_{2.5}$ increases the risk of respiratory diseases, including pneumonia, asthma, and bronchitis, especially in children [13–15].

Recent studies on humans also found that short-term exposure to air pollution interfered with inflammatory responses in healthy volunteers, and this impact varied according to individuals' characteristics. Hassanvand et al. (2017) found that older volunteers (> 65 years old) showed significantly higher levels of high-sensitivity C-reactive protein (hs-CRP) after $PM_{2.5}$ exposure, whereas no significant increase was observed in younger healthy volunteers [16]. Lee et al. (2018) also observed a significant increase in inflammation and coagulation-related cytokines after $PM_{2.5}$ exposure, particularly in individuals with a history of chronic obstructive pulmonary disease (COPD) [17]. Additionally, the effects of different air pollutants on increases in inflammatory biomarkers vary; for example, carbon monoxide (CO) is associated with increases in leukocytes and neutrophils, whereas sulfur dioxide (SO_2) is associated with a decrease in leukocytes and neutrophils [17]. Although research has found a correlation between air pollution exposure and inflammation markers as well as white blood cell (WBC) indices in blood, the impact on pediatric patients, especially those with asthma, remains unclear. Among blood cell tests, absolute neutrophil count (ANC) is an indicator of systemic inflammation, lymphocytes represent T-cell mediated immune responses, eosinophils are associated with allergic reactions and asthma attacks, and platelet count is an indicator of coagulation and thrombosis [18–20]. Therefore, this study aimed to evaluate the effects of short-term exposure to $PM_{2.5}$, and other air pollutants, on blood cell counts, especially ANC, lymphocyte, eosinophil, and platelet count, in pediatric patients with asthma.

Methods

Study population

This retrospective observational study was conducted between January 1, 2007, and December 31, 2018, at an urban tertiary medical center with an average of 73,000 emergency department (ED) visits annually. Pediatric patients who visited the ED due to asthma exacerbations, had blood tests conducted, and resided in Kaohsiung were included in our study. The medical records of non-trauma patients under 17 years of age who visited the ED with a primary diagnosis of asthma (ICD-9: 493 or ICD-10: J45-J46) were extracted from the ED administrative database. Data on age, sex, and underlying co-morbidities, including hypertension, diabetes, malignancy, heart disease, respiratory disease, liver disease, and neurological disease, were collected from the patients' medical records. Blood tests, including WBC count, ANC, eosinophil count, and platelet count, were also recorded. ANC was calculated by multiplying the total WBC by the percentage of neutrophils. This study was approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB NO: 202101652B0) in accordance with the guidelines of the Declaration of Helsinki. Owing to the retrospective nature of this study, informed consent was not required.

Pollutant and meteorological data

Air pollutant data and information regarding meteorological conditions were obtained from 11 air quality monitoring stations in Kaohsiung City established in 1994 by the Taiwanese Environmental Protection Administration. During the study period, the hourly concentrations of five "criteria" pollutants, namely PM_{10} and $PM_{2.5}$ (measured using beta-ray absorption), NO_2 and SO_2 (measured using ultraviolet fluorescence), and O_3 (measured using ultraviolet photometry), were measured. Coarse particulate matter (PM_C, defined as particulate matter with an aerodynamic diameter of 2.5 μm to 10 μm) was calculated by concentration of PM_{10} minus the concentration of $PM_{2.5}$. Weather conditions, including temperature and relative humidity, were also monitored. The daily average concentrations of air pollutants and weather conditions

Table 1 Demographic characteristics of patients

All	Number = 4717 (100%)
Demographic characteristics of patients	
Age (mean ± SD)	(5.4 ± 3.3)
Sex	
Male	3059 (64.9)
Female	1658 (35.1)
Hypertension	64 (1.4)
Neurologic disease	22 (0.5)
Liver disease	152 (3.2)
Malignancy	9 (0.2)
Season	
Warm	2080 (44.1)
Cold	2637 (55.9)
Triage	
I&II	2949 (62.5)
III to V	1768 (37.5)
Admission	3183
ICU	106

SD: standard deviation; warm season: April to September; cold season: October to March; ICU: intensive care unit; Triage I and II indicate a more urgent situation

were then calculated. Patients' addresses were collected from their medical records, and the 24-h average levels of these pollutants were computed based on data from the nearest monitoring station.

Statistical analysis

Continuous variables were expressed as medians with interquartile ranges (25th and 75th percentiles) or mean ± standard error, depending on whether they followed a normal distribution. Since age, gender, and weather conditions may influence the health effects caused by $PM_{2.5}$, multiple linear regression analyses were conducted on complex samples to examine the relationship between air pollutants and blood cell count, adjusting for these confounding factors [21, 22]. The day of an asthma emergency visit was represented as lag0, the day before as lag1, and so on. Due to the prominent 0–6 day lag effect of $PM_{2.5}$ on health, we collected air pollution data for lag 0–6 in this study [22]. We categorized air pollutants into quartiles (Q1 to Q4) based on concentration levels and performed ANOVA to conduct linear trend analysis to evaluate whether an increase in air pollutant levels is linearly associated with changes in blood cell indices and minimizes the influence of outliers or extreme values. Statistical significance (two tails) was set at $p < 0.05$. All analyses were conducted using Statistical Product and Service Solutions (version 22.0; IBM, Armonk, NY, United States).

Results

Characteristics of included patients

During the 12-year study period in Kaohsiung, 5,907 pediatric asthma cases were recorded. Of these, 1,058 were excluded because they were either not residents of Kaohsiung City or had incomplete address information. Additionally, 132 patients were excluded owing to missing blood test results. Consequently, 4,717 patients were included in this study. During the study period, 37 cases revisited the emergency department (ED) with a similar diagnosis within 3 days, and each visit was treated as a separate case. Table 1 presents the patients' demographic characteristics. Among them, 3,059 (64.9%) were male, and the mean age was 5.4 ± 3.3 years. A total of 3,183 (67.5%) patients were admitted to the hospital, 106 (2.2%) were admitted to the intensive care unit, and 2,080 (44.1%) visited the ED during the warm season (April–September).

Conditions of meteorology and air pollution

Table 2 presents the air pollutant and weather conditions of Kaohsiung during the study period. The mean levels of $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 were 36.5 μg/m^3, 68.3 μg/m^3, 18.0 parts per billion (ppb), 5.6 ppb, and 29.4 ppb, respectively. Pearson's correlation coefficients between air pollutants and weather conditions in the study period was presented in supplementary Table 1.

Association between air pollutant exposure on blood cell counts

The regression coefficients (S.E.) for changes in ANC, eosinophil count, lymphocyte count, and platelet count in association with a one-unit increase in air pollutant levels are summarized in Table 3. A one-unit increase in $PM_{2.5}$ (regression coefficient = 25.618; S.E. = 5.937; $p < 0.001$), PM_{10} (regression coefficient = 19.97; S.E. =

Table 2 Summary statistics for meteorology, and air pollution in Kaohsiung, 2007–2018

	Minimum	Percentiles			Maximum	Mean	Warm season (Mean ± SD)	Cold season (Mean ± SD)	*p*	IQR
		25%	50%	75%						
$PM_{2.5}$ (μg/m^3)	1.00	19.00	34.00	50.00	162.00	36.45	24.11 ± 15.28	48.64 ± 19.09	< 0.001	31
PM_{10}(μg/m^3)	6.00	40.00	64.00	91.00	724.00	68.33	47.3 ± 23.13	89.19 ± 31.99	< 0.001	51
NO_2 (ppb)	0.31	11.29	16.78	23.81	69.41	17.98	12.93 ± 6.09	23.01 ± 8.14	< 0.001	12.52
SO_2(ppb)	0.10	3.20	4.80	7.00	52.60	5.63	5.04 ± 3.27	6.22 ± 3.81	< 0.001	3.8
O_3(ppb)	2.10	19.30	28.00	37.70	90.70	29.35	27.77 ± 13.5	30.92 ± 12.13	< 0.001	18.4
Temperature(°C)	6.49	22.52	26.47	28.92	34.95	25.46	28.42 ± 2.04	22.49 ± 3.67	< 0.001	6.4
Humidity (%)	30.79	69.98	74.34	778.70	98.95	74.37	75.99 ± 7.19	72.74 ± 7.38	< 0.001	708.72

Table 3 The associations between common air pollutants and blood cells after adjusting gender, age, temperature and humidity

	Absolute Neutrophil Count (1000/μL)			Eosinophil Counts (1000/μL)			Lymphocyte Counts (1000/μL)				Platelet count (1000/μL)	
	Regression coefficient	SE	*p*	Regression coefficient	SE	*p*	Regression coefficient	SE	*p*	Regression coefficient	SE	*p*
$PM_{2.5}$(μg/m^3)												
lag 0	10.736	4.848	0.027	0.531	0.291	0.069	-0.566	1.547	0.714	0.152	0.082	0.065
lag 1	18.838	4.784	< 0.001	0.543	0.289	0.06	-0.911	1.532	0.552	0.255	0.081	0.002
lag 2	21.392	4.737	< 0.001	0.766	0.286	0.008	-2	1.519	0.188	0.232	0.081	0.004
lag 3	15.515	4.778	0.001	0.679	0.288	0.018	-0.298	1.53	0.846	0.265	0.081	0.001
lag 0–2	21.507	5.326	< 0.001	0.760	0.321	< 0.001	-1.368	1.702	0.421	0.265	0.091	0.003
lag 0–6	25.618	5.937	< 0.001	0.859	0.357	0.016	-1.786	1.895	0.346	0.302	0.101	0.003
PM_{10}(μg/m^3)												
lag 0	8.799	2.759	0.001	0.308	0.166	0.064	-0.65	0.88	0.46	0.099	0.047	0.035
lag 1	13.164	2.771	< 0.001	0.4	0.167	0.017	-1.194	0.886	0.178	0.151	0.047	0.001
lag 2	14.333	2.865	< 0.001	0.439	0.173	0.011	-2.226	0.92	0.016	0.13	0.049	0.008
lag 3	12.001	2.822	< 0.001	0.392	0.169	0.021	-1.492	0.902	0.098	0.17	0.048	< 0.001
lag 0–2	15.686	3.183	< 0.001	0.49	0.192	0.011	-1.769	1.018	0.082	0.167	0.054	0.002
lag 0–6	19.970	3.541	< 0.001	0.728	0.213	0.001	-1.784	1.132	0.115	0.229	0.06	< 0.001
NO_2(ppb)												
lag 0	29.398	13.24	0.026	0.684	0.797	0.391	-4.033	4.229	0.34	0.092	0.225	0.682
lag 1	32.696	12.828	0.011	0.847	0.772	0.273	-4.064	4.085	0.32	0.3	0.217	0.167
lag 2	61.626	12.478	< 0.001	1.628	0.753	0.031	-7.86	3.99	0.049	0.473	0.212	0.026
lag 3	56.809	12.613	< 0.001	1.319	0.757	0.082	-4.92	4.027	0.222	0.464	0.214	0.031
lag 0–2	56.307	14.523	< 0.001	1.385	0.875	0.113	-6.996	4.629	0.131	0.41	0.247	0.097
lag 0–6	70.681	15.857	< 0.001	1.798	0.956	0.06	-8.433	5.054	0.095	0.505	0.27	0.061
SO_2(ppb)												
lag 0	13.637	24.5	0.578	0.87	1.478	0.556	-3.083	9.89	0.696	0.328	0.416	0.431
lag 1	44.184	24.485	0.083	2.473	1.517	0.103	-1.98	8.089	0.807	0.885	0.431	0.04
lag 2	40.407	23.388	0.084	3.627	1.395	0.009	-6.676	7.438	0.369	0.033	0.396	0.933
lag 3	66.068	24.430	0.007	3.771	1.457	0.01	0.86	7.783	0.912	0.399	0.416	0.337
lag 0–2	45.37	27.785	0.103	3.098	1.659	0.062	-5.671	8.844	0.521	0.52	0.471	0.27
lag 0–6	81.694	30.339	0.007	4.086	1.811	0.024	-6.742	9.649	0.485	0.683	0.515	0.185
O_3(ppb)												
lag 0	7.736	7.102	0.276	0.684	0.424	0.107	-0.057	2.258	0.98	0.168	0.121	0.165
lag 1	10.506	6.979	0.132	0.695	0.417	0.095	-1.277	2.219	0.565	0.091	0.118	0.444
lag 2	13.098	6.76	0.053	0.467	0.405	0.248	-0.335	2.155	0.877	0.232	0.115	0.043
lag 3	7.87	6.067	0.234	0.523	0.396	0.187	-2.681	2.106	0.203	0.149	0.112	0.186
lag 0–2	14.611	7.93	0.065	0.827	0.473	0.081	-0.843	2.522	0.738	0.21	0.135	0.12
lag 0–6	23.42	8.831	0.008	0.636	0.528	0.229	-3.507	2.811	0.212	0.227	0.15	0.131

3.541; $p<0.001$), NO_2 (regression coefficient = 70.681; S.E. = 15.857; $p<0.001$), SO_2 (regression coefficient = 81.694; S.E. = 30.339; $p=0.007$), and O_3 (regression coefficient = 23.42; S.E. = 8.831; $p=0.008$) on lag 0–6 correlated positively with ANC. Similarly, increment in $PM_{2.5}$ (regression coefficient = 0.859; S.E. = 0.357; $p=0.016$), PM_{10} (regression coefficient = 0.728; S.E. = 0.213; $p=0.001$), and SO_2 (regression coefficient = 4.086; S.E. = 1.811; $p=0.024$) on lag 0–6 correlated positively with eosinophil counts. Additionally, a one-unit increase in $PM_{2.5}$ (regression coefficient = 0.302; S.E. = 0.101; $p=0.003$) and PM_{10} (regression coefficient = 0.229; S.E. = 0.06; $p<0.001$) on lag 0–6 correlated positively with platelet count.

A two-pollutant model was used to determine which individual contaminants influenced blood cell counts independently of other pollutant effects. In accordance with the results obtained from the single-pollutant models, multi-pollutant models were fitted using different pollutant combinations (with up to two pollutants per model) to assess the stability of the effects of air pollutants. The results are summarized in Table 4. In the two-pollutant model, the results of $PM_{2.5}$ adjusted for PM_{10} are not presented because the variance inflation factor value exceeded 5 in the collinearity diagnostics. Instead, PM_C (particulate matter with an aerodynamic diameter of 2.5 μm to 10 μm) was used for adjustment in the two-pollutant model to evaluate whether $PM_{2.5}$ or PM_C independently affected the various blood cell counts. A μg/m^3 increase in $PM_{2.5}$ was significantly related to the ANC after adjusting for PM_C (regression coefficient = 17.42; S.E. =6.326), SO_2 (regression coefficient = 24.02; S.E. =6.954, $p=0.001$), and O3 (regression coefficient = 23.1; S.E. =6.62, $p<0.001$). A μg/m^3 increase in PM_C was significantly related to the ANC after adjusting for $PM_{2.5}$ (regression coefficient = 23.006; S.E. =6.126, $p<0.001$), NO_2 (regression coefficient = 21.392; S.E. =6.499, $p=0.001$), SO_2 (regression coefficient = 26.581; S.E. =5.941, $p<0.001$), and O3(regression coefficient = 27.075; S.E. =5.952, $p<0.001$). After adjusting for $PM_{2.5}$ (regression coefficient = 48.852; S.E. =20.407, $p=0.017$), PM_C (regression coefficient = 44.408; S.E. =17.983, $p=0.014$), SO_2 (regression coefficient = 94.915; S.E. =20.833, $p<0.001$), and O_3 (regression coefficient = 69.062; S.E. =15.904, $p<0.001$), NO_2 was significantly related to the ANC. In addition, PM_C was significantly associated with eosinophil count after adjusting for $PM_{2.5}$ (regression coefficient = 0.949; S.E. =0.368, $p=0.01$), NO_2 (regression coefficient = 1.046; S.E. =0.391, $p=0.007$), SO_2 (regression coefficient = 0.939; S.E. =0.355, $p=0.008$), and O_3 (regression coefficient = 1.116; S.E. =0.357, $p=0.002$). $PM_{2.5}$ correlated positively with platelet count after adjusting for PM_C, NO_2, SO_2, and O_3. PM_C also correlated positively with platelet count after adjusting for $PM_{2.5}$, NO_2, SO_2, and O_3. The association between NO_2, SO_2, O_3, and platelet count was not statistically significant after adjusting for $PM_{2.5}$ or PM_C.

Table 4 Two pollutants model: the associations of combined effects between common air pollutants (lag 0–6) and absolute neutrophil count

	Absolute Neutrophil Count				
	Adjust $PM_{2.5}$	Adjust PMc	Adjust NO_2	Adjust SO_2	Adjust O_3
$PM_{2.5}$(β, SE)		17.42 (6.326)**	14.187 (7.616)	24.02 (6.954)**	23.1 (6.620)***
PM_C(β, SE)	23.006 (6.126)***		21.392 (6.499)**	26.581 (5.941)***	27.075 (5.952)***
NO_2(β, SE)	48.852 (20.407)*	44.408 (17.983)*		94.915 (20.833)***	69.062 (15.904)***
SO_2(β, SE)	22.39 (35.423)	49.487 (31.361)	-10.599 (39.697)		79.712 (30.369)**
O_3(β, SE)	8.476 (9.819)	13.592 (9.112)	21.287 (8.820)*	22.972 (8.831)**	
	Eosinophil Counts				
	Adjust $PM_{2.5}$	Adjust PMc	Adjust NO_2	Adjust SO_2	Adjust O_3
$PM_{2.5}$(β, SE)		0.509 (0.382)	0.717 (0.458)	0.48 (0.416)	0.811 (0.397)*
PM_C(β, SE)	0.949 (0.368) *		1.046 (0.391)**	0.939 (0.355)**	1.116 (0.357)**
NO_2(β, SE)	0.611 (1.229)	0.448 (1.088)		0.368 (1.250)	1.793 (0.957)
SO_2(β, SE)	2.855 (2.118)	2.828 (1.881)	3.633 (2.377)		4.027 (1.810)*
O_3(β, SE)	0.116 (0.589)	0.198 (0.547)	0.582 (0.529)	0.548 (0.526)	
	Platelet Counts				
	Adjust $PM_{2.5}$	Adjust PMc	Adjust NO_2	Adjust SO_2	Adjust O_3
$PM_{2.5}$(β, SE)		0.216 (0.108)*	0.306 (0.130)*	0.325 (0.118)*	0.287 (0.113)*
PM_C (β, SE)	0.239 (0.104)*		0.294 (0.111)**	0.298 (0.101)**	0.292 (0.102)**
NO_2(β, SE)	-0.017 (0.348)	0.112 (0.307)		0.470 (0.354)	0.482 (0.271)
SO_2(β, SE)	-0.203 (0.602)	0.248 (0.534)	0.104 (0.675)		0.664 (0.516)
O_3(β, SE)	0.044 (0.167)	0.122 (0.155)	0.212 (0.150)	0.216 (0.150)	

* $p<0.05$, ** $p<0.01$, *** $p<0.001$

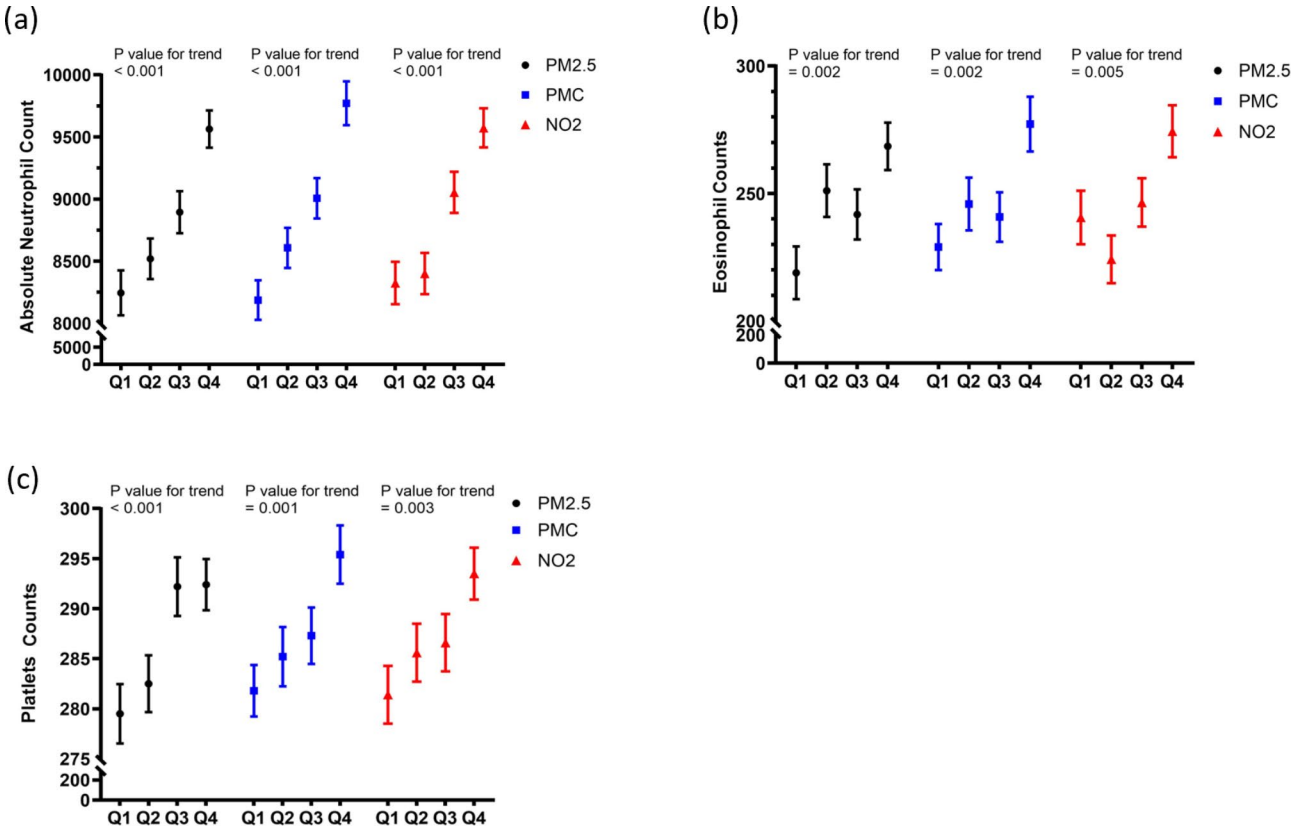

Fig. 1 The linear trend analysis and correlations between the quartiles of each air pollutant and blood cell counts. (**a**) Absolute Neutrophil Count (**b**) Eosinophil Counts (**c**) Platelet Counts

Correlations between the quartiles of air pollutants and blood cell counts

The linear trend analysis and correlations between the quartiles of each air pollutant and blood cell counts are shown in Fig. 1. With increasing quartiles of $PM_{2.5}$ (p-value for trend < 0.001), PM_C (p-value for trend < 0.001), and NO_2 (p-value for trend < 0.001) levels, the mean ANC increased significantly (Fig. 1a). With increasing quartiles of $PM_{2.5}$ (p-value for trend = 0.002), PM_C (p-value for trend = 0.002), and NO_2 (p-value for trend = 0.005) levels, the mean eosinophil count significantly increased (Fig. 1b). Furthermore, as the quartiles of $PM_{2.5}$ (p-value for trend < 0.001), PM_C (p-value for trend = 0.001), and NO_2 (p-value for trend = 0.003) increased, the platelet count increased significantly (Fig. 1c). We also have included the scatter plots illustrating the associations between $PM_{2.5}$, PM_C, NO_2 and ANC, eosinophil counts, and platelet counts in Supplementary Fig. 1.

Discussion

This study found a statistically significant association between air pollutant exposure and blood cell counts in pediatric patients with asthma. After adjusting for confounding factors and other air pollutants, the levels of $PM_{2.5}$, PM_C, and NO_2 correlated positively with ANC, PM_C level correlated positively with eosinophil levels, and $PM_{2.5}$ and PM_C levels correlated positively with platelet levels. In addition, quartile increases in the levels of $PM_{2.5}$, PM_C, and NO_2 correlated positively with ANC, with differences of approximately 13.8%, 16.2%, and 13.0% between the upper and lower quartiles, respectively. Quartile increases in the levels of $PM_{2.5}$, PM_C, and NO_2 correlated positively with eosinophil count by approximately 18.5%, 17.3, and 12.3%, respectively. Furthermore, quartile increases in the levels of $PM_{2.5}$, PM_C, and NO_2 correlated positively with platelet count, with differences of approximately 4.4%, 4.6%, and 4.1% between the upper and lower quartiles, respectively.

Asthma is a common disease in pediatric EDs. According to the International Study of Asthma and Allergies in Childhood, approximately 14% of children worldwide are likely to have experienced asthma symptoms in the past year [23]. Air pollution may be a risk factor contributing to the incidence of pediatric asthma [24]. Numerous epidemiological studies have shown a positive correlation between air pollution exposure and the risk of ED visits for pediatric asthma [25–27]. However, the specific air pollutants that increase the risk of asthma remain unclear. For example, Bouazza et al. collected data from

20 EDs, comprising 47,107 pediatric asthma cases and various air pollutant measurements, including $PM_{2.5}$, PM_{10}, NO_2, and O_3 measurements. The results showed that only $PM_{2.5}$ had a positive correlation with the risk of asthma-related emergency visits, while the impact of other air pollutants was not statistically significant [28]. Another study collected data from 2,507 pediatric patients who visited a hospital for asthma. The results revealed a positive correlation between $PM_{2.5}$, PM_{10}, and NO_2 levels and the risk of hospital visits for asthma. However, the impact of O_3 on hospital visits for asthma was not statistically significant [29]. A review paper collected 20 studies on the correlation between air pollution and asthma exacerbation and conducted a meta-analysis. $PM_{2.5}$ and NO_2 had stronger associations with asthma exacerbation in children, whereas the effects of PM_{10} and O_3 did not reach statistical significance [30]. The present study found that $PM_{2.5}$, PM_C, and NO_2 correlated positively with ANC and eosinophil count. ANC is typically associated with the body's inflammatory response, whereas eosinophils are usually related to allergic reactions and allergic asthma [18, 19]. The results suggest that exposure to air pollution may disrupt the regulation of immune responses in children, potentially increasing the risk of asthma.

Several toxicological studies have indicated that both short- and long-term exposure to air pollution can lead to pulmonary inflammation [31, 32]. Molecular evidence suggested that reactive oxygen species-dependent pathways play a crucial role in the health effects of air pollution, leading to increased oxidative stress in the lungs [33, 34]. These inflammatory and oxidative stress-related cytokines, such as endotoxins and histamine, can enter other organs through the systemic circulation. Meanwhile, ultrafine particles (particles with a diameter less than 0.1 μm) and some lipophilic components of $PM_{2.5}$, such as polycyclic aromatic hydrocarbons (PAHs), can directly cross vascular barriers and enter the systemic circulation, further increasing oxidative stress and systemic inflammatory responses in extra-pulmonary organs such as the kidneys, liver, and heart [33, 35, 36]. The inflammatory response in the lungs, along with inflammation and oxidative stress-related cytokines that enter the systemic circulation, may further influence leukocyte differentiation. Studies on humans have also found that exposure to $PM_{2.5}$, PM_{10}, and PM_C leads to increased levels of inflammation-related cytokines, such as interleukin (IL)-6, in the blood, hs-CRP, and WBC counts [16]. Our results also showed a positive correlation between air pollutant exposure and its impact on the white cell count distribution. The pulmonary and systemic inflammatory responses induced by these air pollutants may further impair lung function, thereby exacerbating asthma attacks. Studies on humans have also shown that exposure to $PM_{2.5}$ is associated with decreased lung function indicators, including the on-second forced expiratory volume (FEV1), forced vital capacity (FVC), and ratio between these two (FEV1/FVC) [37]. Another study collected data from 70 Chinese children and found that, after adjusting for SO_2 and O_3, per 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with approximately a 1.6% decrease in FVC and FEV1 [38]. The disruption of inflammatory responses in children caused by air pollution, along with its impact on lung function, may further exacerbate asthma severity. Epidemiological studies have shown a positive correlation between $PM_{2.5}$ and NO_2 exposure and the risk of asthma-related ED visits and hospitalizations [39, 40]. Additionally, research has indicated that exposure to $PM_{2.5}$ is positively associated with the length of stay for children hospitalized with asthma [41]. These results indicate the hazardous effects of air pollution on asthma exacerbations and adverse outcomes.

The present study found a positive association between $PM_{2.5}$, PM_C, and NO_2 and ANC, eosinophil, and platelet counts in pediatric patients with asthma. Recent studies have shown that exposure to air pollution may disrupt the expression of inflammatory cells, coagulation-related cells, and cytokines in the human body. However, the extent of these effects may vary according to individuals' characteristics and the types of air pollutants. Hassanvand et al. (2017) found that, in older volunteers (>65 years), hs-CRP levels increased significantly following $PM_{2.5}$ exposure, whereas younger healthy volunteers did not exhibit a notable increase [16]. Another study observed significant increases in inflammation and coagulation-related cytokines following $PM_{2.5}$ exposure, particularly in individuals with a history of COPD. The effects of different air pollutants on the elevation of inflammatory biomarkers varied. For instance, CO was associated with increased WBC and neutrophil count, whereas SO_2 was associated with decreased counts [17]. Furthermore, Rich et al. (2012) collected blood biomarkers from 125 healthy volunteers and analyzed their changes before, during, and after the Beijing Olympics. During the Olympics, owing to government regulations on air pollution, $PM_{2.5}$ concentrations dropped from an average of 100.9 $\mu g/m^3$ to 69.4 $\mu g/m^3$, SO_2 levels decreased from 35 ppb to 24 ppb, and NO_2 levels declined from 35 ppb to 33 ppb. Concurrently, soluble P-selectin (sCD62P) decreased by 34.0%, and von Willebrand factor (vWF) decreased by 13.1%. Moreover, the percentage of volunteers with CRP concentrations above the detectable limit (0.3 mg/L) decreased from 55% before the Olympics to 46% during the Olympics [42]. In Taiwan, Hung et al. collected data from volunteers residing near air quality monitoring stations and analyzed the association between air pollution and blood inflammatory markers. The results showed that CO correlated

positively with total WBC, neutrophils, monocytes, and lymphocytes, while SO_2 correlated negatively with WBC, neutrophils, and monocytes [43]. There are several possible reasons for the differences beyond individual characteristics. First, the health effects of different $PM_{2.5}$ compositions appear to vary. Animal studies have found that both the water extract and insoluble particles of $PM_{2.5}$ caused liver damage in mice. However, the water extract primarily induced liver hyperplasia, while the particles mainly caused inflammation and apoptosis [44]. Epidemiological studies have also revealed that higher levels of PAHs in $PM_{2.5}$ are associated with an increased risk of asthma ED visits [45]. A study on humans collected data from 44 volunteers aged > 65 years living in school dormitories and 40 young healthy volunteers. They were exposed to PM from various sources, including industrial emissions, road dust, and vehicle exhaust. The study found significant increases in WBC, vWF, and tumor necrosis factor-soluble receptor-II (sTNFRII) in the blood samples of elderly participants, whereas no significant changes were observed in young healthy participants. Additionally, PM from industrial emissions and road dust had a more pronounced effect on WBC, vWF, and sTNFRII, whereas PM from vehicle exhaust did not have a statistically significant impact on these markers [46]. Another possible reason is that certain components of $PM_{2.5}$ may have synergistic effects with other air pollutants and climatic conditions. Xiao et al. (2016) found that the combined effects of O_3 and the nitrate and sulfate components in $PM_{2.5}$ could be associated with an increased risk of pediatric pneumonia [47]. In another study, exposure to $PM_{2.5}$ was associated with morning hypertension, and this effect was exacerbated by lower temperatures [48]. However, studies on the effects of air pollution on immune cells and platelets in pediatric populations remain limited, with relatively small case numbers. Li et al. collected data from 163 children living in areas with high air pollution exposure and 110 children in the control group, analyzing immune-related cells and biomarkers. The results showed a significant decrease in B lymphocyte count ($p = 0.021$) and levels of Complement Component 3 (C3) and Complement Component 4 (C4) in the exposure group, while monocyte count and the proportion of CD8 + T lymphocytes increased in the exposure group [49]. Another study enrolled 43 children with asthma and calculated their personal exposure. The results showed that increased PM2.5 exposure on lag 1 was associated with increased resistance in both the small and total airways, as well as an elevation in the airway inflammation marker, fractional exhaled nitric oxide [50]. Our results also show that exposure to $PM_{2.5}$, PM_C, and NO_2 was positively correlated with ANC and eosinophil levels in pediatric asthma patients visiting the emergency department. These findings might suggest that such exposures influence the immune response in children with asthma, potentially further impacting airway resistance and increasing the risk of asthma exacerbations.

Our study found that exposure to $PM_{2.5}$ and PM_C was positively associated with platelet count in pediatric patients with asthma. Platelets play important roles in coagulation and thrombosis. Animal studies have shown that co-exposure to silica nanoparticles and lead acetate led decreased anticoagulant function indicators such as thrombin time, prothrombin time, activated partial thromboplastin time, and tissue-type plasminogen activator, as well as an increase in coagulation-related factors such as fibrinogen [51]. Similarly, in a meta-population study including 3,275 participants, long-term increases in $PM_{2.5}$ were matched with significantly increased CRP levels and platelet counts [52]. Xu et al. (2019) collected data from 73 healthy adults and conducted a three-year follow-up study. They found that increases in $PM_{2.5}$ were significantly associated with decreases in tissue inhibitors of matrix metalloproteinases (TIMP-1 and TIMP-2), which led to increased thrombogenicity. This was also related to elevated levels of biomarkers of platelet activity, such as the soluble CD40 ligand and soluble P-selectin [53]. However, numerous prevalence studies have found that exposure to $PM_{2.5}$ was associated with an increased risk of cardiovascular and cerebrovascular diseases [54, 55]. These findings suggest that exposure to air pollution is linked to the activation of coagulation functions and an increased number and activation of platelets, which may subsequently increase the risk of cardiovascular events.

Conclusions

In the present study, we found a statistically significant association between air pollution and ANC and eosinophil and platelet count in pediatric patients with asthma. After adjusting for confounding factors and other air pollutants, the levels of $PM_{2.5}$, PM_C, and NO_2 were found to correlate positively with ANC levels, the PM_C level was positively associated with eosinophil levels, and the $PM_{2.5}$ and PM_C levels were positively associated with platelet levels. In addition, quartile increases in the levels of $PM_{2.5}$, PM_C, and NO_2 correlated positively with ANC, with differences of approximately 13.8%, 16.2%, and 13.0% between the upper and lower quartiles, respectively. Additionally, quartile increases in the levels of $PM_{2.5}$, PM_C, and NO_2 correlated positively with eosinophil and platelet counts. Our results highlight the impact of air pollution on immunity and coagulation in pediatric patients with asthma.

Limitations

This study had some limitations. First, the data were collected from Kaohsiung, an industrial city in a tropical region. The results may differ from those of cities

with different climatic conditions or levels of air pollution. Second, asthma diagnoses were based on clinical judgment, which can vary among physicians, potentially leading to case underreporting and affecting the results. Third, the study did not record the time spent on indoor and outdoor activities or the use of personal protective equipment, which may have resulted in discrepancies between estimated and actual air pollution exposure.

Abbreviations

ANC	absolute neutrophil count
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
FEV1	forced expiratory volume in one second
FVC	forced vital capacity
hs	CRP-high-sensitivity c-reactive protein
ICU	intensive care unit
IL	interleukin
IQR	interquartile range
NO_2	nitrogen dioxide
O_3	ozone
PAHs	polycyclic aromatic hydrocarbons
PM	particulate matter
PM_{10}	particulate matter with an aerodynamic diameter less than 10 μm
$PM_{2.5}$	particulate matter with an aerodynamic diameter less than 2.5 μm
PM_C	coarse particulate matter (2.5–10 μm)
ppb	parts per billion
SD	standard deviation
SO_2	sulfur dioxide
TIMP	tissue inhibitor of metalloproteinase
vWF	von Willebrand factor
WBC	white blood cell

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-21517-w.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

We appreciate the statistical support provided by the Biostatistics Center of Kaohsiung Chang Gung Memorial Hospital.

Author contributions

K. -C. H. and F. -J. C. conceived the manuscript, performed the analyses, and wrote the manuscript. T. -M. H. was contributed to data collection and measurements. H. -Y. P. was involved mainly in data analysis and quality management. C. -C. C. contributed to the revisions of the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding

This study was supported in part by research grants from Kaohsiung Chang Gung Memorial Hospital (grant number CMRPG8N0711). The sponsor played no role in the study design, data collection, analysis, interpretation, writing of the report, or the decision to submit the article for publication.

Data availability

Air pollutant data and meteorological data used and analyzed were acquired from https://airtw.moenv.gov.tw/, which is an open public access. The database of patients used and analyzed during the current study were acquired from Kaohsiung Chang Gung Memorial Hospital. The database were available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB NO: 202101652B0) and was conducted according to the tenets of the 1964 Declaration of Helsinki and its later amendments. The need for informed consent was waived owing to the retrospective nature of the study.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

Received: 4 July 2024 / Accepted: 17 January 2025
Published online: 24 January 2025

References

1. Cheng FJ, et al. Association between ambient air pollution and out-of-hospital cardiac arrest: are there potentially susceptible groups? J Expo Sci Environ Epidemiol. 2020;30(4):641–9.
2. Tian Y, et al. Short-term effects of ambient fine particulate matter pollution on hospital visits for chronic obstructive pulmonary disease in Beijing, China. Environ Health. 2018;17(1):21.
3. Baneras J, et al. Short-term exposure to air pollutants increases the risk of ST elevation myocardial infarction and of infarct-related ventricular arrhythmias and mortality. Int J Cardiol. 2018;250:35–42.
4. Jia Y, et al. Effect of Air Pollution on Heart failure: systematic review and Meta-analysis. Environ Health Perspect. 2023;131(7):76001.
5. Peden DB. Respiratory Health effects of Air pollutants. Immunol Allergy Clin North Am. 2024;44(1):15–33.
6. Mahakalkar AU, et al. Geospatial analysis of short-term exposure to air pollution and risk of cardiovascular diseases and mortality-A systematic review. Chemosphere. 2024;353:141495.
7. Kim T-Y, et al. Short-term effects of ambient PM2.5 and PM2.5-10 on Mortality in Major Cities of Korea. Aerosol Air Qual Res. 2018;18(7):1853–62.
8. Liu H, et al. Ambient particulate matter concentrations and hospitalization for stroke in 26 Chinese cities: a case-crossover study. Stroke. 2017;48(8):2052–9.
9. Wu Y, et al. Seasonal variations, source apportionment, and Health Risk Assessment of Heavy Metals in PM2.5 in Ningbo, China. Aerosol Air Qual Res. 2019;19(9):2083–92.
10. Tsai M-T, et al. Effects of Fine Particulate Matter and its components on emergency room visits for Pediatric Pneumonia: a time-stratified case-crossover study. Int J Environ Res Public Health. 2021;18(20):10599.
11. Walker CLF, et al. Global burden of childhood pneumonia and diarrhoea. Lancet. 2013;381(9875):1405–16.
12. Xing YF, et al. The impact of PM2.5 on the human respiratory system. J Thorac Dis. 2016;8(1):E69–74.
13. Huang M, et al. Source apportionment of primary and secondary PM2.5: associations with pediatric respiratory disease emergency department visits in the U.S. state of Georgia. Environ Int. 2019;133(Pt A):105167.
14. Bono R, et al. Air pollution, aeroallergens and admissions to pediatric emergency room for respiratory reasons in Turin, northwestern Italy. BMC Public Health. 2016;16:722.
15. Marsal A, et al. Prenatal exposure to PM2.5 oxidative potential and lung function in infants and preschool- age children: a prospective study. Environ Health Perspect. 2023;131(1):17004.
16. Hassanvand MS, et al. Short-term effects of particle size fractions on circulating biomarkers of inflammation in a panel of elderly subjects and healthy young adults. Environ Pollut. 2017;223:695–704.
17. Lee H, et al. Short- and long-term exposure to ambient air pollution and circulating biomarkers of inflammation in non-smokers: a hospital-based cohort study in South Korea. Environ Int. 2018;119:264–73.
18. Wechsler ME, et al. Eosinophils in Health and Disease: a state-of-the-art review. Mayo Clin Proc. 2021;96(10):2694–707.
19. Guthrie GJ, et al. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. Crit Rev Oncol Hematol. 2013;88(1):218–30.

20. Yeung J, Li W, Holinstat M. Platelet signaling and disease: targeted therapy for thrombosis and other related diseases. Pharmacol Rev. 2018;70(3):526–48.
21. Chang CH et al. Ambient air Pollution and Risk for Stroke hospitalization: impact on susceptible groups. Toxics, 2022. 10(7).
22. Dong J, et al. Association between atmospheric PM(2.5) and daily outpatient visits for children's respiratory diseases in Lanzhou. Int J Biometeorol. 2021;65(7):989–99.
23. Mallol J, et al. The International Study of Asthma and allergies in Childhood (ISAAC) Phase three: a global synthesis. Allergol Immunopathol (Madr). 2013;41(2):73–85.
24. Madaniyazi L, Xerxes S. Outdoor air pollution and the onset and exacerbation of asthma. Chronic Dis Transl Med. 2021;7(2):100–6.
25. Ho YN, et al. Fine particulate matter constituents associated with emergency room visits for pediatric asthma: a time-stratified case-crossover study in an urban area. BMC Public Health. 2021;21(1):1593.
26. Tiotiu AI et al. Impact of Air Pollution on Asthma outcomes. Int J Environ Res Public Health, 2020. 17(17).
27. Zhang Y, Yin X, Zheng X. The relationship between PM2.5 and the onset and exacerbation of childhood asthma: a short communication. Front Pediatr. 2023;11:1191852.
28. Bouazza N, et al. Fine particulate pollution and asthma exacerbations. Arch Dis Child. 2018;103(9):828–31.
29. Ding L, et al. Air pollution and asthma attacks in children: a case-crossover analysis in the city of Chongqing, China. Environ Pollut. 2017;220(Pt A):348–53.
30. Orellano P, et al. Effect of outdoor air pollution on asthma exacerbations in children and adults: systematic review and multilevel meta-analysis. PLoS ONE. 2017;12(3):e0174050.
31. Lin CI, et al. Instillation of particulate matter 2.5 induced acute lung injury and attenuated the injury recovery in ACE2 knockout mice. Int J Biol Sci. 2018;14(3):253–65.
32. Cakmak S, et al. The influence of polycyclic aromatic hydrocarbons on lung function in a representative sample of the Canadian population. Environ Pollut. 2017;228:1–7.
33. Pardo M, et al. Seasonal variations in fine particle composition from Beijing prompt oxidative stress response in mouse lung and liver. Sci Total Environ. 2018;626:147–55.
34. Kurlawala Z, et al. Fine particulate matter (PM2.5)-Induced Pulmonary oxidative stress contributes to changes in the plasma lipidome and liver transcriptome in mice. Toxicol Sci. 2023;192(2):209–22.
35. Yuan CS, et al. Kidney damage induced by repeated fine particulate matter exposure: effects of different components. Sci Total Environ. 2022;847:157528.
36. Olivo CR, et al. The effects of exercise training on the lungs and cardiovascular function of animals exposed to diesel exhaust particles and gases. Environ Res. 2022;203:111768.
37. Isiugo K, et al. Indoor particulate matter and lung function in children. Sci Total Environ. 2019;663:408–17.
38. Zhou J et al. The effects of short-term PM(2.5) exposure on pulmonary function among children with Asthma-A panel study in Shanghai, China. Int J Environ Res Public Health, 2022. 19(18).
39. Zhou X, et al. Associations between air pollutant and pneumonia and asthma requiring hospitalization among children aged under 5 years in Ningbo, 2015–2017. Front Public Health. 2022;10:1017105.
40. Varghese D, et al. Outdoor air pollution and near-fatal/fatal asthma attacks in children: a systematic review. Pediatr Pulmonol. 2024;59(5):1196–206.
41. Baek J et al. Association between Ambient Air Pollution and Hospital length of stay among children with asthma in South Texas. Int J Environ Res Public Health, 2020. 17(11).
42. Rich DQ, et al. Association between changes in air pollution levels during the Beijing olympics and biomarkers of inflammation and thrombosis in healthy young adults. JAMA. 2012;307(19):2068–78.
43. Hung SC et al. The Association of White Blood Cells and Air Pollutants-A Population-based study. Int J Environ Res Public Health, 2021. 18(5).
44. Yuan C-S, et al. Repeated exposure to fine particulate matter constituents lead to liver inflammation and proliferative response in mice. Ecotoxicol Environ Saf. 2021;224:112636.
45. Hsu SC, et al. Differential time-lag effects of ambient PM(2.5) and PM(2.5)-bound PAHs on asthma emergency department visits. Environ Sci Pollut Res Int. 2020;27(34):43117–24.
46. Altuwayjiri A, et al. Association of systemic inflammation and coagulation biomarkers with source-specific PM2.5 mass concentrations among young and elderly subjects in central Tehran. J Air Waste Manag Assoc. 2021;71(2):191–208.
47. Xiao Q, et al. Pediatric emergency department visits and ambient air pollution in the U.S. State of Georgia: a case-crossover study. Environ Health. 2016;15(1):115.
48. Imaizumi Y, Eguchi K, Kario K. Coexistence of PM2.5 and low temperature is associated with morning hypertension in hypertensives. Clin Exp Hypertens. 2015;37(6):468–72.
49. Li X, et al. Air pollution exposure and immunological and systemic inflammatory alterations among schoolchildren in China. Sci Total Environ. 2019;657:1304–10.
50. He L, et al. Associations of personal exposure to air pollutants with airway mechanics in children with asthma. Environ Int. 2020;138:105647.
51. Feng L, et al. Co-exposure subacute toxicity of silica nanoparticles and lead acetate on cardiovascular system. Int J Nanomed. 2018;13:7819–34.
52. Viehmann A, et al. Long-term residential exposure to urban air pollution, and repeated measures of systemic blood markers of inflammation and coagulation. Occup Environ Med. 2015;72(9):656–63.
53. Xu H, et al. Extreme levels of Air Pollution Associated with changes in biomarkers of atherosclerotic plaque vulnerability and thrombogenicity in healthy adults. Circ Res. 2019;124(5):e30–43.
54. Yen CC, Chen PL. Regional air pollution severity affects the incidence of acute myocardial infarction triggered by short-term pollutant exposure: a time-stratified case-crossover analysis. Environ Sci Pollut Res Int. 2022;29(6):8473–8.
55. Huang JB et al. Association between Air Pollution and Short-Term Outcome of ST-Segment Elevation myocardial infarction in a Tropical City, Kaohsiung, Taiwan. Toxics, 2023. 11(6).

Publisher's note