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Association between Air Pollution and Risk of Hospital Admission for Pediatric Pneumonia in a Tropical City, Kaohsiung, Taiwan

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ABSTRACT

Recent evidences have shown that particulate matter (PM) and other air pollutants are associated with pulmonary and systemic inflammation; however, the relationship between air pollutants and the risk of admission for pediatric pneumonia has not been well surveyed. This study aimed to estimate the hazards of air pollutants on the risk of pediatric pneumonia emergency department (ED) visits and hospitalization. Data on $PM_{2.5}$ (PM with an aerodynamic diameter smaller than 2.5 μm), PM_{10} (PM with an aerodynamic diameter smaller than 10 μm), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) in each of the 11 air monitoring stations in Kaohsiung city were collected. The medical records of non-traumatic patients under 17 years of age who had visited the ED between 2008 to 2013, with a principal diagnosis of pneumonia were extracted. We evaluated the relationship between air pollutant exposure and the risk of admission and length of hospital stay (LOS). An interquartile range increments of $PM_{2.5}$ (odds ratio [OR]: 1.677, 95% confidence interval [CI]: 1.381–2.041), PM_{10} (OR: 1.568, 95% CI: 1.312–1.880), NO_2 (OR: 1.383, 95% CI: 1.179–1.625), SO_2 (OR: 1.261, 95% CI: 1.170–1.361), and O_3 (OR: 1.182, 95% CI: 1.024–1.366) were statistically significantly associated with the risk of pediatric pneumonia hospitalization on lag 0–3. In the two-pollutant model, after adjusting for NO_2 (OR: 1.534, 95% CI: 1.206–1.958), SO_2 (OR: 1.534, 95% CI: 1.206–1.958), or O_3 (OR: 1.741, 95% CI: 1.385–2.196), $PM_{2.5}$ was still statistically significantly associated with pediatric pneumonia hospitalization. Furthermore, higher $PM_{2.5}$ concentration (> 45 μg m^{-3}) was associated with prolonged hospital LOS (OR: 0.217, 95% CI: 0.03–0.404, $P = 0.023$), especially for younger children (≤ 5 years). In conclusion, we found that $PM_{2.5}$, PM_{10}, and SO_2 exposure were risk factors for hospitalization due to pediatric pneumonia.

Keywords: Particulate matter, Pneumonia, Pediatric, $PM_{2.5}$, Air pollution

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1 INTRODUCTION

Many epidemiologic studies have demonstrated a positive association between air pollution and the risk of human diseases, especially respiratory and cardiovascular diseases (Ghaffari *et al.*, 2017; Tsai *et al.*, 2021; Weichenthal *et al.*, 2017). Toxicological studies also found that exposure to air pollutants might induce airway inflammation and elevated systemic circulating inflammatory biomarkers elevation (Dadvand *et al.*, 2014; Lin *et al.*, 2018; Rich *et al.*, 2012). Furthermore, several previous multi-city studies have revealed seasonal and regional variations in air pollution as health hazards (Bell *et al.*, 2008; Peng *et al.*, 2005). There are a few reasons that might partly

explain the seasonal and regional disparities, such as community characteristics (Bell *et al.*, 2008), age of residents (Katsouyanni *et al.*, 2001), and the weather conditions of the community (Ho *et al.*, 2021). Another possible explanation is the different effects of air pollutants. For example, nitrogen dioxide (NO_2) was found to be associated with hospitalization for cardiovascular disease, but the influence of sulfur dioxide (SO_2) was not statistically significant (Ito *et al.*, 2011). Among the air pollutants, fine particulate matter is defined as particulate matter (PM) with an aerodynamic diameter of < 2.5 μm. $PM_{2.5}$ is concerned with health and regulation, and epidemiological studies suggest that $PM_{2.5}$ is more toxic than other air pollutants (Cheng *et al.*, 2019b; Kang *et al.*, 2016; Lv *et al.*, 2017).

Pneumonia is the leading cause of pediatric morbidity and mortality. In 2011, the global incidence of pneumonia in children younger than 5 years was approximately 120 million cases, resulting in approximately 1.3 million child deaths (Walker *et al.*, 2013). Pneumonia is a condition characterized by lung inflammation. Toxicological evidence has shown that exposure to air pollutants might also induce lung inflammation and inflammatory cell accumulation (Lin *et al.*, 2018; Liu *et al.*, 2017). Besides, PM_{10} exposure was found to modify the pulmonary inflammatory reactions induced by the influenza virus, thus significantly elevating the viral titers and exacerbating pulmonary influenza infection in an animal study (Clifford *et al.*, 2015). A recent study also showed that $PM_{2.5}$ and PM_{10} increment was associated with increased COVID-19 infection rates and mortality (Czwojdzinska *et al.*, 2021). For pneumonia, a previous study also showed that air pollution exposure was associated with a higher rate of invasive respiratory or vasopressor support or both in adults (Chen *et al.*, 2020a). In addition, epidemiological studies have revealed a positive association between air pollution and the risk of pediatric pneumonia emergency department (ED) visits and hospitalization (Cheng *et al.*, 2019a; Nhung *et al.*, 2017). However, the association between air pollution and short-term outcomes of pediatric pneumonia is not well understood. As a result, these data were linked to air pollution, weather conditions, and short-term outcomes of pediatric pneumonia to clarify two specific objectives: (1) the short-term outcome between air pollution and pediatric pneumonia; and (2) the association between length of hospital stay of pediatric patients with pneumonia and air pollution.

2 METHOD

2.1 Study Population

This was a retrospective observational study conducted between January 1, 2008, and December 31, 2013, in an urban tertiary medical center in Kaohsiung, Taiwan, with 2,500 beds, with an annual average of 72,000 ED visits. The medical records of non-traumatic pediatric patients under 17 years of age who visited the ED with a principal diagnosis of pneumonia ([International Classification of Diseases, ninth revision (ICD-9]: 480–486) were extracted from the ED administrative database. We included patients clinically diagnosed with pneumonia and their electronic charts were reviewed by two trained physicians. Patients who did not reside in Kaohsiung City or those who transferred to other hospitals were excluded. In addition, sex, age, and prognostic factors for pediatric pneumonia, including diabetes, malignancy, cerebral palsy, respiratory disease (i.e., asthma, chronic respiratory failure), predisposition, insult, response, and organ dysfunction (PIRO) score, renal insufficiency, and shock index were collected from the patients' medical records (Huang *et al.*, 2021; Rello *et al.*, 2009).

2.2 Pollutant and Meteorological Data

During the study period, 11 monitoring stations for air quality were established in Kaohsiung City in 1994 by the Taiwanese Environmental Protection Administration (EPA), a central governmental agency. Air pollutants were measured as previously described (Cheng *et al.*, 2019b). In brief, the stations used commercial monitoring instruments designated by the United States EPA as an equivalent or reference method and manufactured by the US Thermo Environmental Instruments, Inc. (Franklin, MA, USA). The monitoring stations were fully automated, routinely and hourly monitored 5 "criteria" pollutants, including PM_{10}, $PM_{2.5}$ (beta-ray absorption), nitrogen dioxide (NO_2) (ultraviolet fluorescence), sulfur dioxide (SO_2) (ultraviolet fluorescence), and ozone (O_3) (ultraviolet photometry) levels. In addition, the patient's address was collected

from the medical record, 24 h average levels of these pollutants, temperature, and mean humidity from the nearest monitoring station were recorded. The concentration of each air pollutant and temperature and humidity values sampled on the same day of the patient's ED visit were labeled as lag 0. The values sampled on the previous day for the patient who visited the ED were labeled as lag 1. The average concentration of lag 0 to 3 was labeled as lag 0–3. The primary study outcome was patients who required admission, and the secondary outcome was the length of hospital stay (LOS).

2.3 Statistics

The results of the descriptive analyses of the independent variables were reported as percentages or means ± standard deviations (SDs). Independent variables were analyzed using the χ^2, Mann-Whitney U, and Student's t-tests. We used Kolmogorov–Smirnov and Shapiro–Wilk tests to examine the normality of continuous variables. Besides, we assumed that short-term exposure to air pollution was positively related to hospital LOS (days). Therefore, hospital LOS was considered a continuous variable. A linear regression model was used to estimate the effect of air pollution on hospital LOS after adjusting for climate and patient-level characteristics. Statistical significance was set at $P < 0.05$. Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

3 RESULTS AND DISCUSSION

During the six years of the study period, there was a total of 4,047 pediatric patients who visited our ED for pneumonia. A total of 415 patients were excluded from the analysis because they did not reside in Kaohsiung city, while 46 patients were excluded due to incomplete data or transfer to another hospital. The remaining 3,586 patients were included in this study, and 2,726 patients (76.0%) required admission. The demographic characteristics and air pollution conditions in each group are listed in Table 1. Younger children ($P = 0.005$), those with renal insufficiency ($P = 0.029$), cerebral palsy ($P = 0.003$), respiratory disease ($P < 0.001$), and higher PIRO score (≥ 3) for pediatric pneumonia severity ($P < 0.001$) had a higher risk of requiring hospitalization. Patients who required admission had higher $PM_{2.5}$ from lag 0 to 3 ($P < 0.001$, $P < 0.001$, $P < 0.001$, and $P < 0.003$), and the average from lag 0 to 3 (lag 0–3, $P < 0.001$). Patients who required admission also had higher PM_{10}, NO_2, and SO_2 levels on lag 0 to 3, as well as lag 0–3.

3.1 Air Pollutants and Meteorological Results

A summary of meteorological factors, daily mean concentrations of air pollutants, and weather variables in Kaohsiung during the study period is shown in Table 2. The average $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 concentrations over the study period were 43.0 μg m^{-3}, 71.9 μg m^{-3}, 19.3 ppb, 6.7 ppb, and 29.0 ppb, respectively.

3.2 Association between Air Pollutants Exposure and Hospitalization

A binary logistic regression model was used to examine the association between air pollutant exposure and the risk of pediatric pneumonia hospitalization. As shown in Fig. 1, after adjusting for age, renal insufficiency, cerebral palsy, PIRO ≥ 3, and meteorological factors, such as temperature and humidity, and interquartile range (IQR) increments of $PM_{2.5}$ (OR: 1.677, 95% CI: 1.381–2.041), PM_{10} (OR: 1.568, 95% CI: 1.312–1.880), NO_2 (OR: 1.383, 95% CI: 1.179–1.625), SO_2 (OR: 1.261, 95% CI: 1.170–1.361), and O_3 (OR: 1.182, 95% CI: 1.024–1.366) were statistically significantly associated with the risk of pediatric pneumonia hospitalization on lag 0–3.

A two-pollutant model of lag 0–3 was conducted to determine which individual pollutants were independently associated with the risk of pediatric pneumonia hospitalization. In accordance with the results obtained from the single-pollutant models, the multi-pollutant models were fitted with different pollutant combinations (up to two pollutants per model). The results are shown in Fig. 2. After adjusting for NO_2 (OR: 1.534, 95% CI: 1.206–1.958), SO_2 (OR: 1.534, 95% CI: 1.206–1.958), or O_3 (OR: 1.741, 95% CI: 1.385–2.196), $PM_{2.5}$ was still statistically significantly associated with pediatric pneumonia hospitalization. PM_{10} was significantly associated with pediatric pneumonia hospitalization after adjusting for NO_2 (OR: 1.431, 95% CI: 1.150–1.793), SO_2 (OR: 1.351, 95% CI:

Table 1. Demographic characteristics of 3,586 ED pediatric patients with pneumonia.

Characteristics	Admission	Discharge	*P*
	N = 2,726	N = 860	
Male	1,449	461	0.818
Age	4.9 ± 3.5	5.3 ± 3.9	0.005
Diabetes	1	4	0.835
Renal insufficiency	0	15	0.029
Malignancy	0	6	0.169
Leukemia	1	18	0.055
Cerebral palsy	96	13	0.003
Respiratory disease	256	27	< 0.001
PIRO score ≥ 3	116	3	< 0.001
Abnormal shock index	1581	480	0.313
$PM_{2.5}$, μg m^{-3}			
lag 0	44.7 ± 18.6	41.1 ± 18.7	< 0.001
lag 1	44.7 ± 20.3	40.6 ± 18.6	< 0.001
lag 2	45.0 ± 20.9	41.4 ± 18.9	< 0.001
lag 3	45.4 ± 20.7	43.0 ± 19.9	0.003
lag 0–3	44.9 ± 18.1	41.6 ± 16.6	< 0.001
PM_{10}, μg m^{-3}			
lag 0	79.1 ± 37.0	73.1 ± 33.1	< 0.001
lag 1	79.3 ± 36.3	72.2 ± 32.6	< 0.001
lag 2	80.4 ± 43.1	73.8 ± 32.9	< 0.001
lag 3	80.6 ± 37.0	76.4 ± 35.0	0.003
lag 0–3	79.8 ± 32.7	73.9 ± 29.7	< 0.001
NO_2, ppb			
lag 0	21.0 ± 8.7	19.7 ± 7.8	< 0.001
lag 1	21.0 ± 8.7	19.7 ± 8.0	< 0.001
lag 2	21.1 ± 8.7	20.1 ± 8.0	0.003
lag 3	21.4 ± 8.7	20.3 ± 8.0	0.001
lag 0–3	21.1 ± 7.9	19.9 ± 7.2	< 0.001
SO_2, ppb			
lag 0	7.4 ± 5.5	6.4 ± 3.8	< 0.001
lag 1	7.4 ± 5.4	6.2 ± 3.4	< 0.001
lag 2	7.4 ± 5.6	6.3 ± 3.6	< 0.001
lag 3	7.5 ± 3.8	6.4 ± 3.8	< 0.001
lag 0–3	7.4 ± 5.0	6.3 ± 3.2	< 0.001
O_3, ppb			
lag 0	28.4 ± 12.8	27.4 ± 12.3	0.035
lag 1	28.5 ± 13.0	27.5 ± 12.7	0.043
lag 2	28.6 ± 13.0	27.3 ± 12.4	0.008
lag 3	28.7 ± 12.9	28.0 ± 13.0	0.78
lag 0–3	28.6 ± 10.7	27.5 ± 10.4	0.013

ED, emergency department; PIRO score, predisposition, insult, response, and organ dysfunction score; PM, particulate matter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone. Categorical variables were analyzed using the χ^2 test. Continuous variables, including air pollutants, were analyzed using the Mann–Whitney U test.

1.121–1.633), and O_3 (OR: 1.580, 95% CI: 1.291–1.942). SO_2 was independently associated with pediatric pneumonia hospitalization after adjusting for $PM_{2.5}$ (OR: 1.209, 95% CI: 1.123–1.310), PM_{10} (OR: 1.208, 95% CI: 1.120–1.310), NO_2 (OR: 1.239, 95% CI: 1.136–1.363), and O_3 (OR: 1.261, 95% CI: 1.169–1.366).

Linear regression analysis was used to examine the association between air pollutants and hospital LOS. The mean concentration of each pollutant was selected as the cut-off point.

Table 2. Summary statistics for meteorology and air pollution in Kaohsiung, 2008–2013.

	Minimum	Percentiles			Maximum	Mean
		25%	50%	75%		
$PM_{2.5}$ (μg m^{-3})	10.8	24.8	42.3	56.3	126.7	43.0 ± 20.2
PM_{10} (μg m^{-3})	14.7	44.2	71.9	97.2	582.0	74.1 ± 35.1
NO_2 (ppb)	3.9	13.5	18.7	24.6	45.2	19.3 ± 7.1
SO_2 (ppb)	2.0	5.1	6.4	8.0	17.2	6.7 ± 2.1
O_3 (ppb)	3.5	18.9	27.9	37.4	74.6	29.0 ± 12.4
Temperature (°C)	12.4	22.3	26.4	28.7	32.1	25.3 ± 4.2
Humidity (%)	44.0	70.0	74.2	78.1	95.3	74.1 ± 7.2

SD: standard deviation; PM: particulate matter; NO_2: nitrogen dioxide; SO_2: sulfur dioxide; O_3: ozone.

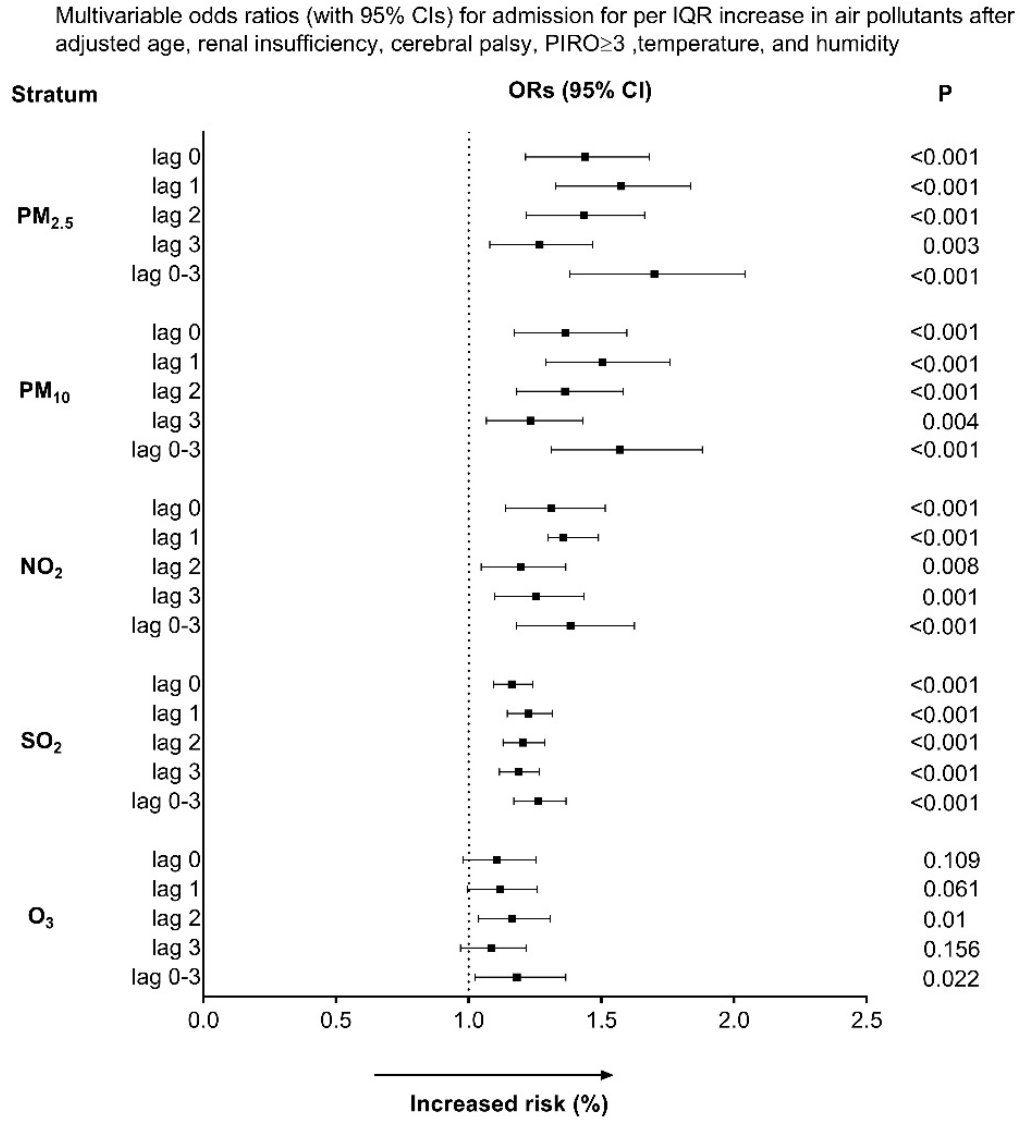

Fig. 1. Multivariate ORs (95% CIs) for admission per IQR increase in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 after adjusting for age, renal insufficiency, cerebral palsy, PIRO ≥ 3, temperature, and humidity.

As shown in Table 3, an average level of $PM_{2.5}$ (lag 0–3) > 45 μg m^{-3} was associated with prolonged hospital LOS (OR: 0.217, CI: 0.03–0.404, P = 0.023). For younger children (≤ 5 years), the influence of $PM_{2.5}$ on hospital LOS was more obvious (OR: 0.250, CI: 0.038–0.463, P = 0.021). The impact of PM_{10}, SO_2 on pediatric pneumonia hospital LOS was not statistically significant. The risk of

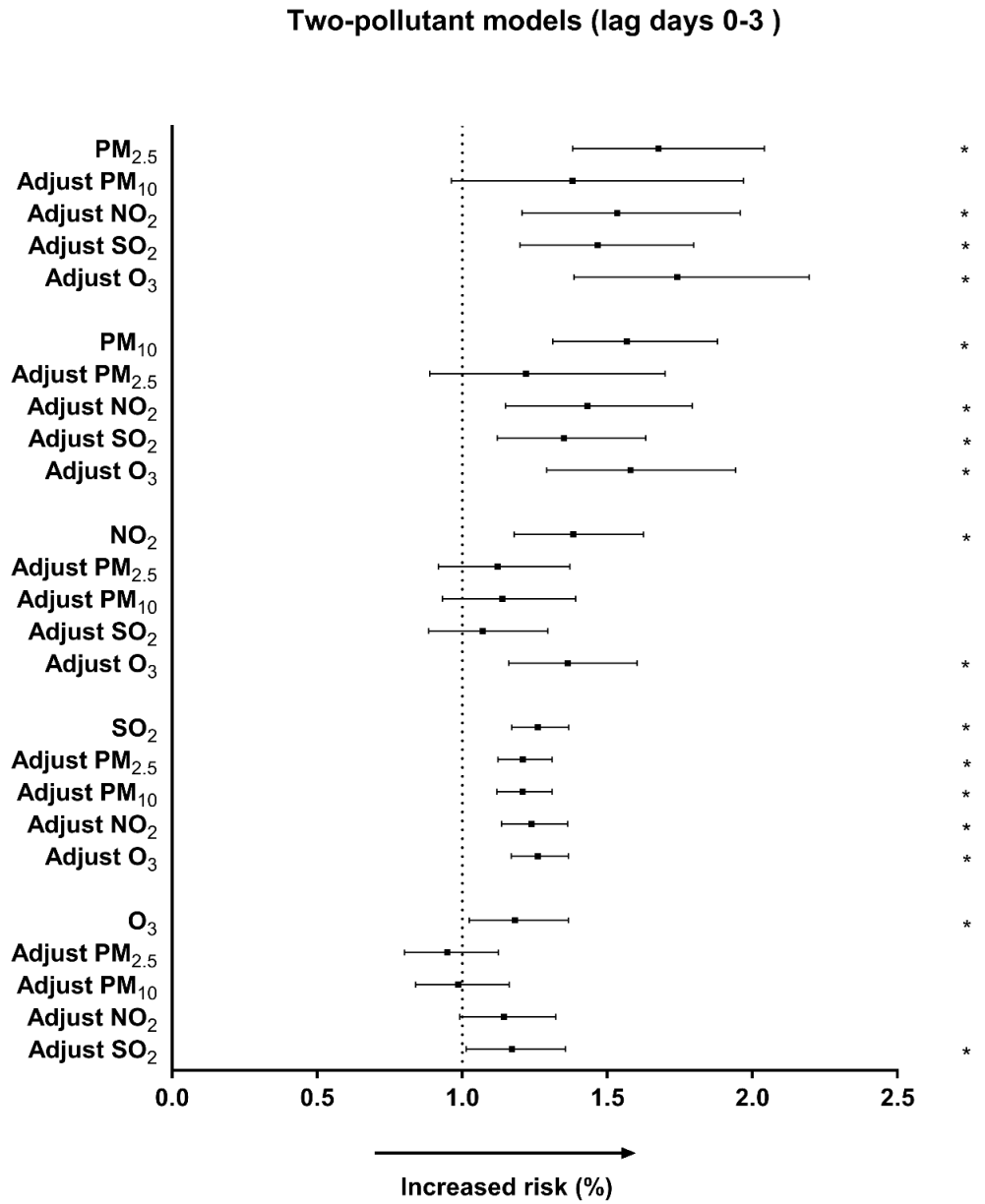

Fig. 2. OR for pediatric pneumonia admission, after adjusting for age, renal insufficiency, cerebral palsy, PIRO $\geq$ 3, temperature, and humidity, for each interquartile range change in the two-pollutant models.

pediatric pneumonia hospitalization increased when the average concentration on lag 0–3 of $PM_{2.5}$ > 45 μg m^{-3} (OR: 1.456, CI: 1.202–1.766, $P < 0.001$), PM_{10} > 80 μg m^{-3} (OR: 1.431, CI: 1.181–1.737, $P = 0.002$), and SO_2 > 7.4 ppb (OR: 0.250, CI: 0.038–0.463, $P = 0.021$). The impact of $PM_{2.5}$, PM_{10}, and SO_2 on hospitalization was more obvious in younger children ($\leq$ 5 years), and the effects of $PM_{2.5}$, PM_{10}, and SO_2 did not achieve statistical significance in older children (> 5 years).

In this study, we estimated the effect of air pollutants on the risk of pediatric pneumonia ED visits and hospitalization and found that $PM_{2.5}$, PM_{10}, and SO_2 might be associated with a higher risk for hospital admission, especially for younger children. Furthermore, a higher concentration of $PM_{2.5}$ was associated with prolonged hospital LOS for pediatric pneumonia.

Although several epidemiologic studies have shown that air pollution is associated with the risk of ED visits and hospitalization related to pediatric pneumonia, limited evidence has focused on air pollution and the short-term outcome of respiratory tract infection (Nhung *et al.*, 2017). Toxicologic studies have demonstrated that $PM_{2.5}$ exposure induces inflammatory cell accumulation

Table 3. Multivariable odds ratios (with 95% CIs) for hospital LOS (days) after adjusting for age, renal insufficiency, cerebral palsy, PIRO ≥ 3, temperature, and humidity.

Multivariable odds ratios (with 95% CIs) per IQR increase in air pollutants after adjusting for age, renal insufficiency, cerebral palsy, PIRO ≥ 3, temperature, and humidity													
Odds for hospital LOS					≤ 5 years					> 5 years			
	OR	95% CI for EXP (B)		*P*		OR	95% CI for EXP (B)		*P*		OR	95% CI for EXP (B)		*P*
		Lower	Upper				Lower	Upper				Lower	Upper	
$PM_{2.5}$ lag 0–3 > 45 μg m^{-3}	0.217	0.03	0.404	0.023	$PM_{2.5}$ lag 0–3 > 45 μg m^{-3}	0.25	0.038	0.463	0.021	$PM_{2.5}$ lag 0–3 > 45 μg m^{-3}	0.190	–0.179	0.56	0.312
PM_{10} lag 0–3 > 80μg m^{-3}	0.021	–0.165	0.207	0.824	PM_{10} lag 0–3 > 80 μg m^{-3}	0.037	–0.173	0.247	0.730	PM_{10} lag 0–3 > 80 μg m^{-3}	0.007	–0.364	0.38	0.969
SO_2 lag 0–3 > 7.4 ppb	0.146	–0.016	0.309	0.078	SO_2 lag 0–3 > 7.4 ppb	0.123	–0.064	0.31	0.196	SO_2 lag 0–3 > 7.4 ppb	0.097	–0.218	0.413	0.545
Multivariable odds ratios (with 95% CIs) per IQR increase in air pollutants after adjusting for age, renal insufficiency, cerebral palsy, PIRO ≥ 3, temperature, and humidity													
Odds for admission					≤ 5 years					> 5 years			
	OR	95% CI for EXP (B)		*P*		OR	95% CI for EXP (B)		*P*		OR	95% CI for EXP (B)		*P*
		Lower	Upper				Lower	Upper				Lower	Upper	
$PM_{2.5}$ lag 0–3 > 45 μg m^{-3}	1.456	1.202	1.766	< 0.001	$PM_{2.5}$ lag 0–3 > 45 μg m^{-3}	1.539	1.209	1.961	< 0.001	$PM_{2.5}$ lag 0–3 > 45 μg m^{-3}	1.305	0.947	1.802	0.104
PM_{10} lag 0–3 > 80 μg m^{-3}	1.431	1.181	1.737	0.002	PM_{10} lag 0–3 > 80 μg m^{-3}	1.655	1.302	2.109	< 0.001	PM_{10} lag 0–3 > 80 μg m^{-3}	1.089	0.785	1.509	0.609
SO_2 lag 0–3 > 7.4 ppb	1.500	1.259	1.791	< 0.001	SO_2 lag 0–3 > 7.4 ppb	1.624	1.297	2.042	< 0.001	SO_2 lag 0–3 > 7.4 ppb	1.317	0.992	1.755	0.057

in the alveolar space of rats along with inflammatory cytokine up-regulation in human bronchial epithelial cells (Zou *et al.*, 2020). However, PM_{10} and $PM_{2.5}$ exposure suppress human T-cell mediated anti- Mycobacterium tuberculosis (MTB) immune response, and thus, might exacerbate MTB infection (Ibironke *et al.*, 2019). Furthermore, $PM_{2.5}$ exposure also compromises immune response by suppressing interleukin-1β and interferon-β production during influenza infection thus enhancing the severity of pneumonia (Tao *et al.*, 2020). Similarly, $PM_{2.5}$ exposure suppresses proinflammatory cytokine secretion induced by pneumococcus thus reducing the phagocytic activity of macrophages (Chen *et al.*, 2020b). MTB, virus, and pneumococcus are known major causative agents of pediatric pneumonia. The inflammatory reaction modulated by air pollution might affect the severity of pneumonia. The present study provided clinical evidence supporting the hypothesis that short-term air pollution exposure might affect the outcome of pediatric pneumonia.

Many recent studies have revealed the hazard effects of air pollutants, especially respiratory and cardiovascular diseases, and different air pollutants may have different health effects. For example, $PM_{2.5}$ was found to be associated with pediatric asthma ED visits (Ho *et al.*, 2021), chronic obstructive pulmonary disease (COPD) hospitalization (Liang *et al.*, 2019), admission for myocardial infarction (MI) (Weichenthal *et al.*, 2017), and mortality due to stroke (Shah *et al.*, 2015). In addition, PM_{10} has been found to be associated with the risk of asthma ED visits (Zheng *et al.*, 2015), intracerebral hemorrhage (Han *et al.*, 2016), and acute MI hospitalization (Collart *et al.*, 2017). SO_2 exposure has also been found to be related to COPD exacerbation (DeVries *et al.*, 2016) and admission for acute stroke (Shah *et al.*, 2015). However, there are disparities among the different studies. For example, Collart *et al.* (2017) revealed a positive association between PM_{10}, $PM_{2.5}$, and NO_2 on acute MI hospitalization, but the influence of PM_{10} did not achieve statistical significance in another study (Ghaffari *et al.*, 2017). For pediatric pneumonia, Lv *et al.* (2017) demonstrated a positive association between $PM_{2.5}$ and PM_{10} and pediatric pneumonia hospitalization, even after adjusting for SO_2. Cheng *et al.* (2019a) collected data from 4,024 pediatric patients with pneumonia and found that $PM_{2.5}$ and NO_2 were significantly associated with pneumonia ED visits, even after adjusting for PM_{10} and SO_2. However, Darrow *et al.* (2014) did not observe a statistically significant association between $PM_{2.5}$ mass and pediatric pneumonia ED visits. Strickland *et al.* (2016) only observed a significant association between $PM_{2.5}$, pediatric asthma ED visits, and pediatric pneumonia. One possible reason for this disparity is the different $PM_{2.5}$. The constituents of $PM_{2.5}$ from different emission sources were different. For example, $PM_{2.5}$ produced by the combustion of biomass, motorcycles, and plants is composed of elemental carbon and organic carbon. $PM_{2.5}$ is produced by residual oil combustion, smelters, and oil-fired power plants contain more sulfur and sulfate (Chow, 1995). Therefore, different constituents of $PM_{2.5}$ may induce different health hazards. Although Darrow *et al.* (2014) did not observe a significant influence of $PM_{2.5}$ mass on pediatric pneumonia ED visits, the organic carbon fraction of $PM_{2.5}$ was statistically related to pediatric pneumonia. Another study also found that different $PM_{2.5}$ components might have different hazards in pediatric pneumonia, and the elemental carbon fraction of $PM_{2.5}$ seemed to play a more important role (Tsai *et al.*, 2021). Recently, several toxicological studies have attempted to clarify the health effects of different PM components. Pardo *et al.* (2018) designed an animal experiment and found that organic extracts of $PM_{2.5}$ induced oxidative stress in the mice liver and lungs, especially $PM_{2.5}$, collected during the heating season. This result suggests that polycyclic aromatic hydrocarbons of $PM_{2.5}$ might play an important role in the lung's oxidative stress. Another study also found that the water extract of $PM_{2.5}$ induced signals of proliferation upregulation, but insoluble particles of $PM_{2.5}$ induced inflammatory cytokines in the mouse liver (Yuan *et al.*, 2021). In other words, different $PM_{2.5}$ and $PM_{2.5}$ constituents from different areas and seasons might induce different health effects. Second, the health effects of $PM_{2.5}$ seemed to vary for different groups of patients. Kang *et al.* (2016) revealed that patients of advanced age were more susceptible to $PM_{2.5}$ on out-of-hospital cardiac arrest (OHCA). NO_2 was also found to be associated with the risk of OHCA, especially for those with cardiovascular risk factors (Cheng *et al.*, 2020). A previous study showed that younger children were at the highest risk of pneumonia hospitalization due to airborne PM (Lv *et al.*, 2017). As a result, different studies included different groups of patients, which might also have led to different study results.

Toxicological studies also showed different hazards in different groups of study participants.

Hassanvand *et al.* (2017) compared inflammatory biomarkers after PM exposure among healthy young and older adults and found a significant elevation of highly sensitive C-reactive protein in older adults but not in young adult. Third, patient-level characteristics and weather conditions may also influence PM hazards. For example, cigarette smoking were more susceptible to $PM_{2.5}$ to develop COPD (Su *et al.*, 2021), while low temperature combined with higher $PM_{2.5}$ concentration was associated with a higher risk of morning hypertension (Imaizumi *et al.*, 2015). Nhung *et al.* (2017) enrolled 17 studies and performed a meta-analysis, and they concluded that $PM_{2.5}$ and PM_{10} exposure were statistically significantly associated with the risk of pediatric pneumonia ED visits. The present study also supported the hypothesis that $PM_{2.5}$ and PM_{10} exposure were associated with the risk of pediatric pneumonia hospitalization.

SO_2 exposure is known to induce airway irritation, mucus secretion, and bronchospasm. When SO_2 penetrates the lower respiratory tract, it might convert into bisulfite and interact with sensory receptors, causing bronchoconstriction (Chen *et al.*, 2007). However, the association between SO_2 exposure and the risk of respiratory disease during ED visits remains controversial. Liang *et al.* (2019) collected data on 161,613 COPD hospitalizations during 2013–2017 and found that the SO_2 concentration was associated with the risk of COPD hospitalization. Other epidemiological studies also support the positive association between SO_2 exposure and COPD exacerbation (DeVries *et al.*, 2016; Gao *et al.*, 2019; Santus *et al.*, 2012). However, Orellano *et al.* (2017) collected 22 studies on air pollution on asthma exacerbation, but the hazard effect of SO_2 did not achieve statistical significance after meta-analysis. For pediatric pneumonia, Xiao *et al.* (2016) collected seven years of data from Georgia hospitals in the United States, including 90,063 pneumonia and 148,256 asthma/wheeze ED visits. They demonstrated that SO_2 concentration was positively related to asthma/wheeze ED visits, but SO_2 was not significantly related to pneumonia ED visits (Xiao *et al.*, 2016). However, a review article analyzed 22 studies and found that SO_2 exposure was positively related to pediatric pneumonia ED visits (Nhung *et al.*, 2017). The present study also supports the results that SO_2 exposure on lag 0–3 might increase the risk of pediatric pneumonia hospitalization. Toxicological studies have also supported the hazardous effects of SO_2 on airways. Animal studies have revealed that SO_2 exposure increases airway epithelial permeability, glutathione-S-transferase response, and pulmonary inflammatory reactions (Joelsson *et al.*, 2020; Yun *et al.*, 2011). Pneumonia is a condition characterized by lung inflammation, and SO_2 exposure may strengthen the inflammatory response.

This study has several limitations. First, this was a retrospective observational study that included only one hospital in a single city, and the results may not be generalizable to other locations. Second, this study was conducted in a tropical industrial city, and the results in other cities with different meteorological conditions may be different. Furthermore, factors such as air conditioning usage and time spent outdoors that might affect personal exposure were not included in the present study. These factors may influence the magnitude of the observed associations compared with those at other geographical locations.

4 CONCLUSIONS

In conclusion, we found that $PM_{2.5}$, PM_{10}, and SO_2 exposures were associated with a higher risk of admission for pediatric pneumonia. These effects may be greater in younger children. Furthermore, a higher concentration of $PM_{2.5}$ was associated with prolonged hospital LOS for pediatric pneumonia.

ADDITIONAL INFORMATION AND DECLARATIONS

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Institutional Review Board Statement

This study was approved by the institutional review board of Kaohsiung Chang Gung Memorial Hospital (201801301B0) and conducted in accordance with the ethical guidelines of the 1964

Declaration of Helsinki and its amendments and comparable ethical standards. Informed consent was not required for this study.

Data Availability Statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interests

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