

Short-term Exposure of PM_{2.5} and PM₁₀ Increases the Number of Outpatients with Eczema in Guangzhou: A Time-Series Study

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Abstract

Background: The worldwide prevalence of eczema has continued to rise over the past decades. This has led to emphasis on the association between air pollution and eczema. This study investigated the relationship between daily exposure to air pollution and the number of eczema outpatient visits in Guangzhou with the overarching goal of providing novel insights on the interventions for eczema aggravation and prevention.

Methods: Daily air pollution data, meteorological data, and number of eczema outpatients were obtained from 18th January 2013 to 31st December 2018 in Guangzhou. A generalized additive model with Poisson distribution was used to assess the association between the number of eczema outpatient visits and short-term exposure of PM_{2.5} and PM₁₀. In addition, the effect of PM_{2.5} and PM₁₀ by age (<65 years, ≥65 years) and gender was evaluated.

Results: A total of 293,343 eczema outpatient visits were recorded. The obtained results indicated that a 10µg/m³ increase of the same day/ lag 1 day/ lag 2 days PM_{2.5} was associated with increments of 2.33%(RR=1.0233, 95%CI: 1.0206-1.0260, *P*<0.001), 1.81% (RR=1.0181, 95%CI: 1.0153-1.0209, *P*<0.001), and 0.95%(RR=1.0095, 95%CI: 1.0068-1.0123, *P*<0.001) in eczema outpatients risk, respectively. On the other hand, a 10µg/m³ increase of PM₁₀ was associated with eczema outpatients risk increments of 1.97%(RR=1.0197, 95%CI: 1.0177-1.0217, *P*<0.001), 1.65%(RR=1.0165, 95%CI: 1.0145-1.0186, *P*<0.001), and 0.98%(RR=1.0098, 95%CI: 1.0078-1.0118, *P*<0.001), respectively. Furthermore, the effects of PM on the increment of eczema were similar in the male and female groups. Results obtained after age stratification analyses indicated that the strongest positive association between PM_{2.5} exposure and eczema were observed at lag 0 day with the percent changes being 4.72% (95%CI, 4.18-5.28%, *P*<0.001), 1.92%(95%CI: 1.65-2.19%, *P*<0.001) and 3.34% (95%CI, 2.9- 3.78%, *P*<0.001) in <12 years old, ≥12 and <65years old, and ≥65 years old groups, respectively.

Conclusion: Short-term exposure of PM_{2.5} and PM₁₀ increases the number of eczema outpatients especially among children and the elderly. This study has provided a further understanding of the relationship between air pollutants and eczema, which will benefit disease prevention and lower the health burden.

Background

Eczema is a group of common inflammatory skin diseases. Patients may develop different skin lesions and relapsing pruritus in the different stages, thereby causing considerable physical and psychological burden on the patients¹⁻³. The worldwide prevalence of eczema has been rising continuously over the past decades^{4,5}. The available clinical treatments only improve the symptoms as opposed to curing the disease. Therefore, the lack of a cure for eczema highlights the importance of prevention. A previous study has reported that identification of the underlying modifiable risk factors for eczema including environmental stimuli plays a decisive role in the prophylactic management of the disease⁶.

The rapid development in China has resulted in air pollution becoming worse^{7,8}. Among the many air pollutants, particulate matter (PM) is derived from anthropogenic activities of fossil fuel combustion, mostly contributed by the consumption of fuel by vehicles⁹. PM is a complicated mixture with alternative concentration, particle diameter, and chemical properties in various spaces and time¹⁰. According to the particles' aerodynamic diameter, PM can be categorized into PM_{0.1} (particle diameter ≤ 0.1 µm), PM_{2.5} (particle diameter ≤ 2.5 µm), and PM₁₀ (particle diameter ≤ 10 µm)¹¹. In addition to the genetic background, dietary habits, lifestyle, and societal status have also been associated with the pathogenic condition of skin diseases^{12,13}. Accumulating scientific evidence has reported the effects of PM on the development of eczema and dermatitis^{14,15}. A meta-analysis study reported that an estimated increase of 10 µg/m³ in PM_{2.5} and PM₁₀ can lead to a 1.60% (0.45–2.82) and 1.01% (0.08–2.05) increase of skin diseases risk, respectively¹⁶. However, the study had limited epidemiologic findings, and the existing evidence was inconsistent¹⁷.

Guangzhou is one of the most densely populated cities in China. A previous study reported that PM has become one of the main sources of air pollution in Guangzhou due to the rapid industrial development and advanced transportation¹⁸. Therefore, this study investigated the association between daily air pollution exposure and the number of outpatients with eczema in Guangzhou. Additionally, the above associations were also evaluated in different ages, and gender subgroups. The main aim of the study was to identify the potential environmental risk factors and to provide novel insights on the interventions for eczema aggravation and prevention.

Materials And Methods

Study setting

Guangzhou, the capital city of Guangdong province, is one of the developed cities in China with an approximate population of 14.9 million in 2018. The city, located at 23^o10'N, 113^o18'E, has a typical subtropical humid-monsoon climate with an average annual temperature and rainfall of 22°C and 1500–2000 mm, respectively. In addition, Guangzhou is the top-ranking commercial and manufacturing city in China. Therefore, the problem of air pollution in the city as a result of economic advancement should not be underestimated. In 2019, the average concentrations of PM_{2.5}, PM₁₀, NO₂, SO₂, and O₃ in Guangzhou were 30 g/m³, 53 g/m³, 45 g/m³, 7 g/m³, and 178 g/m³, respectively¹⁹.

Data sources

Patient Data

The Dermatology Hospital of Southern Medical University, located in Tianhe district, Guangzhou, is a large-scale dermatology specialty and brand influence hospital in South China. The hospital has the largest number of eczema outpatient visits in Guangzhou. This study enrolled outpatients who were diagnosed with eczema coded as L30.902 according to the World Health Organization's International Classification of Diseases (the 10th version (ICD-10)) in the hospital from 18th January 2013 to 31st December 2018. If recurrent eczema occurred within 21 days of a previous outpatient visit, it was regarded as a single eczema event.

Air Pollution and Meteorological Data

Air quality monitoring data was obtained from the public sharing system of Guangzhou Environmental Monitoring Center (http://210.72.1.33:8023/gzaqi_new/

RealTimeDate.html). Data recorded in the system was obtained from 11 national air quality monitor stations in Guangzhou and the daily average air quality data was used for our analyses. Daily average concentrations of PM_{2.5}, PM₁₀, NO₂, SO₂, and O₃ during the period ranging from 18th January 2013 to 31st December 2018 were also collected. Daily meteorological data, including mean humidity and temperature, were obtained from the China Meteorological Data Sharing Service System based on data from different meteorological stations in Guangzhou, and used for analyses. Both air pollution and meteorology data followed the quality control programs which are mandated by the Chinese government.

Statistical Analyses

A generalized additive model (GAM) with Poisson distribution was used to assess the association between eczema outpatient visits and short-term exposure of PM_{2.5} and PM₁₀²⁰. Lag 0–3 days were used to explore the cumulative exposure and displacement effects of PM and other pollutants²¹. This study used a single pollutant model to examine the independent association between PM and eczema admission. In addition, we built a two-pollutant model to control the potential confounding effects of other pollutants²². These models can be represented as follows:

$$\log(\mu_t) = \alpha + \sum \beta_i X_{it} + NS(\text{temperature}_t, df = 3) + NS(\text{humidity}_t, df = 3) + NS(\text{time}_t, df = 10 / \text{year}) + \gamma DOW_t$$

where μ_t represents the expected number of eczema outpatients on day t , α is the intercept; X_{it} represents the concentrations of pollutants (PM_{2.5}, PM₁₀, NO₂, SO₂, and O₃) on day t , $i = 1$ or $i = 2$ represents single pollutant model or two-pollutant model respectively; and β_i stands for the coefficient of X_i . A natural cubic spline function (NS) with 10, 3, and 3 degrees of freedom (df) was used to capture the nonlinear relationships of time trend, temperature, and humidity²³. In our model, day of week (DOW_t) was set in the form of categorical variables, while γ represents the effect of DOW_t on eczema outpatients.

Age and gender stratification analyses using potential individual-level effect modifiers were also conducted. This study used the above basic models to examine outcomes by stratification of age (< 65 years, \geq 65 years) and gender for the purpose of exploring the potential modification.

In addition, the dfs for temperature, humidity, and time used in the above models were assessed using Akaike information criterion for quasi-Poisson (Q-AIC). The minimum value of Q-AIC represented the best goodness and the optimum of dfs. In order to check the robustness of our modeling strategies, sensitivity analyses were done by changing the df for temperature (2–4), humidity (2–4), and calendar time (9–11 per year) to control time trend²⁴. R software version 4.0.2 was used to conduct all the analyses and a P value < 0.05 was considered to be statistically significant in all statistical analyses.

Results

Data description

In this study, a total of 293,343 eczema outpatients were recorded in the Dermatology Hospital of Southern Medical University from 18th January 2013 to 31st December 2018. Table 1 shows the descriptive statistics of daily eczema outpatients, air pollutants, and meteorological variables. The average number of daily eczema outpatients in the hospital was 190 in 2018, while the average concentrations of air pollutants including PM_{2.5}, PM₁₀, NO₂, SO₂, and O₃ were 34.7 $\mu\text{g}/\text{m}^3$, 55.7 $\mu\text{g}/\text{m}^3$, 48.1 $\mu\text{g}/\text{m}^3$, 9.6 $\mu\text{g}/\text{m}^3$, and 50.7 $\mu\text{g}/\text{m}^3$, respectively. In addition, the annual mean temperature and humidity were 22.3°C and 81.7%, respectively. With the exception of temperature (F value = 0.313, p value = 0.905), the annual average values of all other variables were significantly different from 2013 to 2018. Furthermore, there was an increased trend of eczema outpatient visits.

Table 1
Daily number of eczema outpatients, meteorological factors, and air pollutants in Guangzhou (2013/1/18-2018/12/31)

	2013	2014	2015	2016	2017	2018	F	P
Eczema outpatients	75.261 ± 23.840	93.688 ± 31.839	131.406 ± 37.233	155.644 ± 43.374	180.638 ± 48.581	190.845 ± 48.430	478.389	< .001
Temperature ^a (°C)	22.160 ± 5.585	21.768 ± 6.580	22.229 ± 5.927	22.019 ± 6.395	22.136 ± 5.837	22.255 ± 6.177	0.313	0.905
Humidity *(%)	81.296 ± 11.546	78.448 ± 10.628	78.057 ± 8.907	81.991 ± 9.698	80.942 ± 11.373	81.685 ± 10.203	9.472	< .001
PM _{2.5} *(mg/m ³)	50.165 ± 27.241	49.350 ± 24.731	38.958 ± 21.112	34.163 ± 17.220	35.033 ± 19.055	34.663 ± 21.135	40.575	< .001
PM ₁₀ *(mg/m ³)	72.139 ± 34.403	67.476 ± 30.655	60.636 ± 28.122	54.739 ± 25.081	56.388 ± 27.007	55.658 ± 27.538	21.298	< .001
NO ₂ *(mg/m ³)	51.237 ± 21.476	44.093 ± 18.826	45.188 ± 17.063	43.716 ± 18.109	49.664 ± 19.595	48.064 ± 19.605	9.315	< .001
SO ₂ *(mg/m ³)	20.798 ± 8.447	20.953 ± 15.474	12.998 ± 5.216	11.954 ± 3.783	11.739 ± 3.645	9.603 ± 3.262	135.621	< .001
O ₃ *(mg/m ³)	61.797 ± 36.736	57.796 ± 33.119	47.715 ± 24.465	47.175 ± 24.994	50.253 ± 27.124	50.678 ± 25.623	14.398	< .001
a F = 0.313, p value = 0.905								
*p value < 0.001								

Obtained results indicated that the correlation coefficients between PM_{2.5} and temperature, humidity, PM₁₀, NO₂, SO₂, and O₃ were 0.32, 0.22, 0.94, 0.73, 0.60, and 0.31, respectively. PM_{2.5} was negatively correlated with temperature and humidity, and positively correlated with PM₁₀, NO₂, SO₂, and O₃. On the other hand, the correlation coefficients between PM₁₀ and temperature, humidity, PM_{2.5}, NO₂, SO₂, and O₃ were 0.24, 0.26, 0.94, 0.80, 0.44, and 0.35, respectively. Similarly, PM₁₀ was negatively correlated with temperature and humidity, and positively correlated with PM_{2.5}, NO₂, SO₂, and O₃. The highest Pearson correlations were observed between PM_{2.5} and PM₁₀ (Supplementary Table 1).

Distributed lag nonlinear model analyses

The smallest Q-AIC of 27558.6 was obtained with per year df of 3, 3, 10 for temperature, humidity, and time, respectively (Supplementary Table 2). This result formed the basis for the distributing lag nonlinear model analyses which followed.

Results obtained from the single pollutant model indicated that a per 10 g/m³ increase of PM_{2.5} led to a 2.33% (RR = 1.0233, 95%CI: 1.0206–1.0260, P < 0.001), 1.81% (RR = 1.0181, 95%CI: 1.0153–1.0209, P < 0.001), 0.95% (RR = 1.0095, 95%CI: 1.0068–1.0123, P < 0.001), and 0.29% (RR = 1.0095, 95%CI: 1.0029–1.0056, P = 0.274) increase in the number of daily eczema outpatients at lag 0–3 days, respectively. In addition, a per 10 g/m³ increase of PM₁₀ caused 1.97% (RR = 1.0197, 95%CI: 1.0177–1.0217, P < 0.001), 1.65% (RR = 1.0165, 95%CI: 1.0145–1.0186, P < 0.001), 0.98% (RR = 1.0098, 95%CI: 1.0078–1.0118, P < 0.001), and 0.52% (RR = 1.0052, 95%CI: 1.0032–1.0071, P = 0.008) increase in the number of daily eczema outpatients at lag 0–3 days, respectively (Table 2).

Table 2
The RR and percent change of eczema risk associated with a 10 mg/m³ increase of PM_{2.5} and PM₁₀

Pollutant(per 10 mg/m ³)	Lag Day	RR	PC (%)	p_value
PM _{2.5}	Lag 0	1.0233 (1.0206–1.0260)	2.33 (2.06–2.6)	< .001
	Lag 1	1.0181 (1.0153–1.0209)	1.81 (1.53–2.09)	< .001
	Lag 2	1.0095 (1.0068–1.0123)	0.95 (0.68–1.23)	< .001
	Lag 3	1.0029 (1.0003–1.0056)	0.29 (0.03–0.56)	0.274
PM ₁₀	Lag 0	1.0197 (1.0177–1.0217)	1.97 (1.77–2.17)	< .001
	Lag 1	1.0165 (1.0145–1.0186)	1.65 (1.45–1.86)	< .001
	Lag 2	1.0098 (1.0078–1.0118)	0.98 (0.78–1.18)	< .001
	Lag 3	1.0052 (1.0032–1.0071)	0.52 (0.32–0.71)	0.008
RR: risk ratio; PC: percentage change				

On the other hand, results obtained from the two-pollutant model analyses indicated that a per 10 g/m³ increase of PM_{2.5} adjusting for PM₁₀, NO₂, SO₂, and O₃ led to a 1.29% (RR = 1.0129, 95%CI: 1.0113–1.0145), 2.01% (RR = 1.0201, 95%CI: 1.018–1.0223), 2.54% (RR = 1.0254, 95%CI: 1.0223–1.0285), and 1.46% (RR = 1.0146, 95%CI: 1.0129–1.016) increase of eczema outpatient visits at lag 0–3 days, respectively. Besides, per 10 g/m³ increase of PM₁₀ increased eczema outpatient visits by 1.75% (RR = 1.0175, 95%CI: 1.0158–1.0192), 2.34% (RR = 1.0234, 95%CI: 1.021–1.0258), and 1.4% (RR = 1.014, 95%CI: 1.0125–1.0154) at lag 0–3 days, respectively, after adjusting for NO₂, SO₂, and O₃(Table 3).

Table 3
The RR and percent change of eczema risk associated with a 10 mg/m³ increase of PM_{2.5} and PM₁₀ under the two-pollutant model

Pollutant(per 10 mg/m ³)	Model type	RR	PC (%)
PM _{2.5} [*]	PM _{2.5} + PM ₁₀	1.0129 (1.0113–1.0145)	1.29 (1.13–1.45)
	PM _{2.5} + NO ₂	1.0201 (1.018–1.0223)	2.01 (1.8–2.23)
	PM _{2.5} + SO ₂	1.0254 (1.0223–1.0285)	2.54 (2.23–2.85)
	PM _{2.5} + O ₃	1.0146 (1.0129–1.0163)	1.46 (1.29–1.63)
PM ₁₀ [*]	PM ₁₀ + NO ₂	1.0175 (1.0158–1.0192)	1.75 (1.58–1.92)
	PM ₁₀ + SO ₂	1.0234 (1.021–1.0258)	2.34 (2.1–2.58)
	PM ₁₀ + O ₃	1.014 (1.0125–1.0154)	1.4 (1.25–1.54)
* <i>p</i> value < 0.001			
RR: risk ratio; PC: percentage change			

Stratification analyses

Results obtained after gender stratification analyses indicated that a 10 µg/m³ increase of PM_{2.5} concentrations caused a 2.32% (95%CI: 2.03–2.61%, *P* < 0.001), 1.77% (95%CI: 1.47–2.07%, *P* < 0.001), 0.9% (95%CI: 0.61–1.19%, *P* = 0.002), and 0.16% (95%CI: -0.13-0.44%, *P* = 0.579) increase in the risk of eczema outpatient visits at lag 0–3 days, respectively, in the male group. On the other hand, the percentage change of eczema outpatients in the female group were 2.31% (95%CI: 2.01–2.61%, *P* < 0.001), 1.82% (95%CI: 1.51–2.13%, *P* < 0.001), 0.99% (95%CI: 0.68–1.29%, *P* = 0.001), and 0.41% (95%CI: 0.12–0.71%, *P* = 0.160) at lag 0–3 days, respectively. In addition, age stratification analyses results indicated that the strongest positive association between PM_{2.5} exposure and eczema were observed at lag 0 day with the percent changes being 4.72% (95%CI, 4.18–5.28%, *P* < 0.001), 1.92% (95%CI: 1.65–2.19%, *P* < 0.001) and 3.34% (95%CI, 2.9–3.78%, *P* < 0.001) in the < 12 years old, ≥ 12 and < 65 years old, and ≥ 65 years old groups, respectively. Gradual weakening trends could be observed at lag 1–3 days.

Furthermore, a 10 µg/m³ increase of PM₁₀ concentrations caused a 1.97% (95%CI: 1.76–2.18%, *P* < 0.001), 1.6% (95%CI: 1.38–1.81%, *P* < 0.001), 0.94% (95%CI: 0.73–1.15%, *P* < 0.001), and 0.39% (95%CI: 0.18–0.6%, *P* = 0.059) increase in the risk of eczema outpatient visits at lag 0–3 days, respectively, in the male group. On the other hand, the percentage change of eczema outpatient visits in the female group were 1.97% (95%CI: 1.75–2.19%, *P* < 0.001), 1.71% (95%CI: 1.48–1.93%, *P* < 0.001), 1.01% (95%CI: 0.79–1.23%, *P* < 0.001), and 0.65% (95%CI: 0.43–0.86%, *P* = 0.002) at lag 0–3 days, respectively. Results obtained after age stratification analyses indicated that the strongest positive association between PM₁₀ exposure and eczema were also observed at lag 0 day with the percent changes being 3.74% (95%CI, 3.34–4.14%, *P* < 0.001), 1.66% (95%CI, 1.47–1.86%, *P* < 0.001), and 2.55% (95%CI: 2.24–2.87%, *P* < 0.001) among the three age groups. Similarly, gradual weakening trends could also be observed at lag 1–3 days (Table 4). In addition, PM_{2.5} and PM₁₀ had similar effects on the number of eczema outpatients in both the two-pollutant model and the single pollutant model (Table 5).

Table 4
Stratification analysis of the percent change of eczema risk associated with a 10 mg/m³ increase of PM_{2.5} and PM₁₀

Pollutant (per 10 mg/m ³)	Lag Day	Male		Female		< 12		12–64		≥ 65	
		PC (%)	p_value	PC (%)	p_value	PC (%)	p_value	PC (%)	p_value	PC (%)	p_value
PM _{2.5}	Lag 0	2.32(2.03–2.61)	< .001	2.31(2.01–2.61)	< .001	4.72(4.18–5.28)	< .001	1.92(1.65–2.19)	< .001	3.34(2.9–3.78)	< .001
	Lag 1	1.77(1.47–2.07)	< .001	1.82(1.51–2.13)	< .001	3.11(2.54–3.68)	< .001	1.59(1.31–1.87)	< .001	2.27(1.82–2.73)	< .001
	Lag 2	0.9(0.61–1.19)	0.002	0.99(0.68–1.29)	0.001	0.91(0.36–1.46)	0.096	0.84(0.57–1.12)	0.002	1.59(1.14–2.03)	< .001
	Lag 3	0.16(-0.13–0.44)	0.579	0.41(0.12–0.71)	0.160	-0.74(-1.26–-0.22)	0.159	0.3(0.03–0.56)	0.26	1.15(0.72–1.59)	0.008
PM ₁₀	Lag 0	1.97(1.76–2.18)	< .001	1.97(1.75–2.19)	< .001	3.74(3.34–4.14)	< .001	1.66(1.47–1.86)	< .001	2.55(2.24–2.87)	< .001
	Lag 1	1.6(1.38–1.81)	< .001	1.71(1.48–1.93)	< .001	2.81(2.4–3.23)	< .001	1.46(1.26–1.66)	< .001	1.9(1.57–2.23)	< .001
	Lag 2	0.94(0.73–1.15)	< .001	1.01(0.79–1.23)	< .001	1.16(0.77–1.56)	0.003	0.88(0.69–1.08)	< .001	1.27(0.95–1.59)	< .001
	Lag 3	0.39(0.18–0.6)	0.059	0.65(0.43–0.86)	0.002	-0.27(-0.64–0.12)	0.485	0.53(0.33–0.72)	0.006	0.99(0.68–1.3)	0.002

PC: percentage change

Table 5
Stratification analysis of the percent change of eczema risk associated with a 10 mg/m³ increase of PM_{2.5} and PM₁₀ under the two-pollutant model

Pollutant (per 10 mg/m ³)	Model type	Male	Female	< 12	12–64	≥ 65
PM _{2.5} *	PM _{2.5} + PM ₁₀	1.24 (1.06–1.41)	1.34 (1.17–1.52)	1.86 (1.54–2.18)	1.13 (0.97–1.3)	1.81 (1.55–2.07)
	PM _{2.5} + NO ₂	1.96 (1.73–2.19)	2.04 (1.81–2.28)	2.65 (2.22–3.08)	1.79 (1.58–2.01)	2.67 (2.32–3.02)
	PM _{2.5} + SO ₂	2.46 (2.12–2.79)	2.6 (2.25–2.94)	3.71 (3.09–4.34)	2.22 (1.91–2.54)	3.65 (3.15–4.16)
	PM _{2.5} + O ₃	1.41 (1.22–1.59)	1.52 (1.33–1.71)	2.55 (2.2–2.89)	1.26 (1.09–1.43)	2.02 (1.74–2.3)
PM ₁₀ *	PM _{2.5} + NO ₂	1.69 (1.51–1.88)	1.8 (1.61–1.99)	2.35 (2–2.7)	1.57 (1.4–1.74)	2.19 (1.91–2.47)
	PM _{2.5} + SO ₂	2.25 (2–2.51)	2.42 (2.15–2.68)	3.38 (2.9–3.87)	2.07 (1.84–2.31)	3.03 (2.64–3.41)
	PM _{2.5} + O ₃	1.34 (1.19–1.5)	1.46 (1.3–1.62)	2.33 (2.03–2.62)	1.22 (1.07–1.37)	1.82 (1.58–2.06)

*pvalue < 0.001

Sensitivity Analyses

The obtained results after sensitivity analyses done in this study showed that the effect estimates of PM_{2.5} and PM₁₀ were not materially influenced by changing the df for the smooth function of time trend indicating the credibility of our results (Supplementary Table 3).

Discussion

This study investigated the correlations between meteorological and environmental factors with the number of eczema outpatient visits in Guangzhou. In total, 293,343 cases of eczema were analyzed using PM_{2.5} and PM₁₀. The obtained results suggested that the increasing concentrations of air pollutants were significantly associated with the rising number of eczema cases. A 10 µg/m³ increase of PM_{2.5} on the same day/ lag 1 day/ lag 2 days was associated with increments of 2.33% (2.06–2.6%), 1.81% (1.53–2.09%), and 0.95% (0.68–1.23%) in the eczema outpatients risk, respectively. Similarly, a 10 µg/m³ increase of PM₁₀ was associated with eczema outpatients risk increments of 1.97% (1.77–2.17%), 1.65% (1.45–1.86%), and 0.98% (0.78–1.18%) at the same day/ lag 1 day/ lag 2 days, respectively.

The number of outpatient visits has been widely used in environmental epidemiology studies to estimate the influence of air pollutants on eczema. The confounders including seasonal changes and long-term trends can be modified using the distributed lag nonlinear model²⁵⁻²⁷. Previous studies conducted in Shanghai and Chengdu, two representative cities with high urbanization in China, have reported that multiple air pollutants in both cities had the potential of increasing the incidence and prevalence of eczema^{28,29}. The conclusions from both studies are consistent with results obtained in this study. In addition, Dong *et al.*, suggested that raising public awareness is crucial for constantly improving the air quality. This is because PM is not only associated with cardiovascular and respiratory issues but it also has a positive connection with the occurrence of skin diseases in China³⁰. Although a decreasing tendency in the levels of PM concentrations was observed from 2013 in the main regions in China including the Beijing-Tianjin-Hubei region, Yangtze River Delta, and Pearl River Delta, the recorded concentration levels still exceeded the limits recommended by the World Health Organization and Chinese authorities³¹. With the acceleration of economic and industrial development, air pollution will most likely be an inevitable issue, particularly in the developing countries.

Generally, identification of vulnerable groups is of great significance for public health prevention. The existing evidences have limitations in revealing whether the effects of air pollution on eczema differ in population subgroups. Therefore, we stratified the eczema cases into three groups including < 12, ≥ 12 and < 65, and ≥ 65 years old. The obtained results indicated that children (< 12) and the elderly (≥ 65) were more vulnerable to adverse effects of short-term exposure to PM. The skin, which is the largest organ in the human body, contains four different barrier components including physical, chemical, microbial, and immunological barriers³². The physical barrier, which mainly consists of the stratum corneum, can exert the protection function against penetration of pathogens, allergens, and several other exogenous air pollutants such as PM, NO₂, and SO₂^{33,34}. A healthy skin barrier plays an essential role of preventing damage caused by stimuli including air pollutants. The vulnerable groups can easily suffer from eczema after short-term exposure to PM due to the immature and aging skin barrier in children and the elderly, respectively. Undeveloped sebaceous glands, skin infections, and local immune dysregulation are the main reasons for epidermal barrier abnormalities in children³⁵⁻³⁷. On the other hand, epidermal dysfunction, compromised permeability homeostasis, reduced stratum corneum hydration, and elevated skin surface pH are the aggressive factors for the elderly^{37,38}. Therefore, this study suggests that children and the elderly should avoid staying outdoors frequently to prevent PM exposure, which will potentially decrease the risk of eczema.

However, the mechanisms of how PM induces and aggravates eczema in humans have not yet been elucidated. It is likely that PM induces the disruption of the epidermis by modulating the structural proteins including small proline-rich (SPRR) family, occludens-1 (ZO-1), keratins, filaggrin, and claudin-1³⁹⁻⁴⁵, thereby resulting in both increased epithelial and endothelial barrier permeability⁴⁶. Moreover, a previous study reported that the penetration of PM was observed in both intact and barrier-disrupted skin *in vivo*, resulting in inflammatory responses⁴⁷. Current scientific opinions on the down-stream mechanisms through which air pollutants affect skin health mainly include: 1) elevation of oxidative stress via exogenous and endogenous reactive oxygen species (ROS) generation, which is a series of a highly reactive chemical substances. Numerous evidences have suggested that PM can induce direct and indirect ROS formation, resulting in lipid, protein, and DNA damage^{10,48,49}; 2) activation of the aryl hydrocarbon receptor (AhR), which further limits cell proliferation and implicates in skin senescence⁵⁰; 3) activation of the inflammatory cascade in skin and impairing of the immunological barrier^{39,43,51}; 4) activation of toll-like receptors, NF- κ B, and MAPK signaling pathways⁵²⁻⁵⁶; and 5) induction of apoptosis and autophagy^{57,58}. Currently, the clinical management strategies for eczema mainly include the administration of moisturizers, topical corticosteroids, and calcineurin inhibitors, representing an anti-allergen and anti-inflammation strategy. Since the skin is the most important defense barrier against environmental contaminants, future research should elucidate the clear mechanism of how air pollutants aggravate eczema in humans with the overarching goal of providing recommendations for improving skin protection against air pollution.

To the best of our knowledge, this is the first study which has uncovered the associations and lagged effects between exposure to environmental factors and number of eczema outpatients in Guangzhou, southern China. However, the study has several potential limitations. Firstly, the study used data on the number of eczema outpatient visits to estimate the effect of exposure to PM rather than using authentic physiological records or measurements. In addition, the clinical cases were only selected from one hospital. Although the hospital selection bias might be inevitable, the Dermatology Hospital of Southern Medical University is one of the largest and representative dermatological departments among the local hospitals. Therefore, it can be used to reflect the trend of eczema outpatient visits from the whole region. Secondly, the data on the exposure of individuals to the environmental factors was unavailable. Furthermore, the outdoor average concentrations of PM_{2.5}, PM₁₀, NO₂, SO₂, and O₃ were recorded as the average obtained from the different fixed monitoring stations, which may raise errors in documented measurements. Thirdly, the study does not include detailed information on the severity of eczema and the differentiation of initial onset or relapsing cases, which may lead to bias while interpreting the results. However, our study still offers considerable evidence on the relationship between environmental factors and the prevalence of eczema, thereby proposing highlights for promoting the policies and actions which will lead to the reduction of air pollution for a better skin condition.

Conclusion

This study has contributed to the limited scientific evidence which suggests that PM_{2.5} and PM₁₀ may induce and aggravate eczema especially among children and the elderly, and has provided considerable public health concerns on skin diseases. The study provided a further understanding of the relationship between air pollutants and eczema, which will aid in disease prevention and lower the health burden.

List Of Abbreviations

PM: particulate matter; GAM: generalized additive model; ICD-10: International Classification of Diseases, the 10th version; DOW: day of week; Q-AIC: Akaike information criterion for quasi-Poisson; SPRR: small proline-rich; ROS: reactive oxygen species; AhR: aryl hydrocarbon receptor

Declarations

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Authors' contributions

SS and JC designed the study. JZ, JX and DJ analyzed the data. YY drafted the manuscript. BS, YC contributed to the data collection. All authors critically reviewed and approved the manuscript.

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Availability of data and materials

The air pollution data that support the findings of this study are available on request from the corresponding author, Qing Chen. The eczema data are not publicly available due to the privacy restriction.

Ethics approval and consent to participate

The protocol of study and accessing the hospital admission data was approved by the ethics committee of Dermatology Hospital, Southern Medical University, and was performed in accordance with the ethical standards noted in the 1964 Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.

Competing interests.

The authors declare they have no competing interests.

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