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ORIGINAL RESEARCH

The Association Between Short-Term Air Pollution Exposure and Post-Adolescent Acne: The Evidence from a Time Series Analysis in Xi'an, China

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Background: Post-adolescent acne is a common skin disease faced by adults. However, whether air pollution (AP) serves as a risk factor for post-adolescent acne remains elusive.
Aim: To determine the relationship between short-term AP exposure (within 7 days) and outpatient visits for post-adolescent acne.
Methods: Daily outpatient visit data for post-adolescent acne and routinely AP data between 2010 and 2013 were collected from Xi'an, China. A generalized additive regression model was used to analyze the relationship between outpatient visits for post-adolescent acne and short-term ambient AP exposure. The gender-specific analyses were conducted as well.
Results: Totally, 27,190 outpatient visits for post-adolescent acne were included. The results revealed that a 10 μg/m^3 increase in PM_{10}, SO_2, and NO_2 at lag 0–7 day was associated with the increase of outpatient visits for post-adolescent acne at 0.84% (95% CI: 0.53%, 1.16%), 1.61% (95% CI: 0.12%, 3.10%), and 3.50% (95% CI: 1.60%, 5.40%), respectively. The significant positive associations of PM_{10}, SO_2, and NO_2 were found at both single-lag models and moving average models. The gender-specific analyses showed that the effect estimates of PM_{10} was stronger for females than for males, while there was no observed gender difference in the effects of SO_2 and NO_2.
Conclusion: Short-term exposure to AP was associated with increased outpatient visits for post-adolescent acne, especially for females in the effects of PM_{10}.
Keywords: short-term, air pollution, post-adolescent acne, adult acne, time-series analysis

Introduction

Acne vulgaris, an inflammatory disease of the pilosebaceous follicles, has been traditionally considered a common skin disease for teenagers.[1] In recent years, the number of adults affected by new-onset acne or persistent acne is gradually rising.[2,3] Approximately 61.9% of populations in the United States[4] and 41% of female individuals in France[5] were found to be affected by acne during their adulthood. It results in with lower qualities of life and negative psychosocial conditions for patients.[6,7]

Especially, acne of adults over 25 years of age is generally defined as post-adolescent acne, which is considered to be a particular subtype of acne differing from adolescent acne.[8] It mainly occurs in females with mild-to-moderate severity. In addition, compared with adolescent acne, post-adolescent acne has more inflammatory lesions and less comedones.[9] Moreover, unlike adolescent acne, which always appears on the forehead, nose, and upper cheeks, post-adolescent acne predominantly occurs on the chin, jawline, and neck.[9]

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Many factors have been thought to be associated with the risk of acne, such as smoking habits,[10] body mass index (BMI),[11] genetic factors,[12,13] and cosmetics,[14] etc. Recent studies stressed that air pollution (AP) has adverse impacts on people's health, especially cardiovascular and pulmonary systems.[15–22] Some studies also take AP's effects into consideration of the induction and aggravation of acne, because AP could contribute to hyper-seborrhea and hyper-sebum, both of which have been found to be prevalent in acne lesions.[23–28] However, given that the clinical features of post-adolescent acne, including the vulnerable population, the degree of inflammation, and the primary parts of bodies, were different from those of adolescent acne, the risk factors reported for acne are necessary to be reclassified and re-identified for both adults and teenagers.[29] Attention should also be paid to the epidemiological evidence regarding the effect of AP on post-adolescent acne.

In this study, time-series analyses were conducted to investigate the association between outpatient visits for post-adolescent acne and daily AP in Xi'an, a northwestern Chinese city with relatively heavy AP. Subgroup analyses were also carried out to investigate the potential gender difference in such association.

Methods

Data for Outpatient Visits

Daily outpatient visit data for post-adolescent acne between 1 October 2010 and 31 December 2013 were obtained from Xijing Hospital in Xi'an, a northwestern Chinese city with an area of 10,108 km^2 and a population of over 8 million in 2014.[30] It has distinct climate fluctuations with four seasons. The medical services of Xijing Hospital are accessible seven days a week. The diagnosis of acne vulgaris (ICD-10: L70) was defined by dermatologists according to Andrews' Diseases of the Skin-Clinical Dermatology (11th edition). Both new acne cases and the relapses of previous diagnosed patients whose residential areas were in Xi'an City and whose ages were over 25 years old were included. The informed consent of patients was not obtained because there was no individual interaction with patients. In addition, the Ethics Committee of Third Military Medical University (Army Military Medical University) approved this study, and the protocols complied with the Declaration of Helsinki.

Environmental Data

AP data between 1 October 2010 and 31 December 2013 were acquired from the Environmental Monitoring Center of Xi'an, including particulate matter less than 10 μm in aerodynamic diameter (PM_{10}), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2). The daily (24-h) mean concentrations were used as metrics of AP exposures, which were calculated by averaging hourly data across 13 monitoring stations covering Xi'an. The data of daily mean temperature and daily relative humidity during the study period were obtained from the local meteorological bureau.

Statistical Analysis

Firstly, the descriptive analyses were performed to characterize the basic information of outpatient visits, AP data, and meteorological data. The generalized additive model (GAM) was conducted to investigate the association between daily AP and outpatient visits for post-adolescent acne because daily outpatient visits followed quasi-Poisson distribution. In such models, the outpatient visits of post-adolescent acne were included as the dependent variable, while daily AP, temperature, and relative humidity were included as independent variables. The formula used for the analyses and the choosing of degrees of freedom (df) were described in detail in our previous studies,[31,32] and the formula was as follows:

$$\log E(Y_t) = \beta Z_t + ns(temp, 6) + ns(RH, 3) + ns(time, 7/year) + DOW_t + intercept$$

Gender-specific analyses were also conducted by Z-test. The estimated differences between gender subgroups were shown by the estimates of differences between groups and their 95% confidence intervals (95% CIs).

Analyses were performed using the "mgcv" package in R 3.6.0 (http://www.r-project.org). The results were presented as the percentage increase of outpatient visits for post-adolescent acne with a 10 $\mu g/m^3$ increase of PM_{10}, SO_2, and NO_2 per day. *P*-values less than 0.05 ($P<0.05$) were considered statistically significant.

Results

Table 1 shows demographic information of daily outpatient visits and environmental factors. Totally, 27,190 outpatient visits for post-adolescent acne were recorded, including 7,587 males and 19,603 females. The average daily outpatient visits were 22.9. During the period, the daily mean concentrations of PM_{10}, SO_2, NO_2 were 142.6 $\mu g/m^3$, 44.7 $\mu g/m^3$, and 48.5 $\mu g/m^3$, respectively. The average daily temperature was 14.3°C and relative humidity was 62.4%.

Table 1 Descriptive Statistics for Daily Outpatient Visits, Concentrations of Air Pollutants, and Weather Conditions

	Mean	Min	Max	P25	P50	P75	SD
Post-adolescent acne	22.9	0.0	60.0	17.0	22.0	28.0	9.1
Gender							
Male	6.4	0.0	20.0	4.0	6.0	8.0	3.4
Female	16.5	0.0	49.0	11.0	16.0	21.0	7.2
Air pollutant concentrations (24-h average)							
PM_{10} (μg/m^3)	142.6	20.0	1020.0	86.0	122.0	166.0	96.2
SO_2 (μg/m^3)	44.7	8.0	202.0	20.0	30.0	60.8	34.9
NO_2 (μg/m^3)	48.5	14.4	141.0	32.0	43.2	60.8	20.9
Mean Temperature (°C)	14.3	−5.5	33.9	5.4	15.3	23.2	10.1
Mean Relative humidity (%)	62.4	16.0	98.0	51.0	63.0	74.8	16.8

Notes: P25, P50, and P75: the 25th, 50th, and 75th percentiles.
Abbreviations: PM_{10}, particulate matter with an aerodynamic diameter less than 10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; SD, standard deviation.

In Figure 1, the time series of outpatient visits, air pollutants, and meteorological factors were shown. The outpatient visits for post-adolescent acne were increasing over time, especially those for female patients. AP was more severe during winter, and there were minor peaks of outpatient visits in the same period. The temperature had a significant undulation period over the year, which was higher during summers. However, the relative humidity showed no apparent seasonal trend.

In Figure 2, the correlations between AP and daily post-adolescent acne outpatient visits in single-lag days (lag 0 to lag 7) and cumulative exposure days (lag 0–1 to lag 0–7) were shown. In single-lag models, the positive association was evidenced from lag 0 to lag 3 and at lag 6 for PM_{10}, at lag 3 for SO_2, and from lag 0 to lag 3 for NO_2. In cumulative exposure models, both PM_{10} and NO_2 showed significant positive associations with outpatient visits for post-adolescent acne from lag0–1 to lag 0–7, while SO_2 had such associations from lag 0–4 to lag 0–7. To be specific, every 10 μg/m^3 increase of PM_{10}, SO_2, and NO_2 was associated with the increase of outpatient acne visits at 0.84% (95% CI: 0.53%, 1.16%), 1.61% (95% CI: 0.12%, 3.10%), and 3.50% (95% CI: 1.60%, 5.40%) at lag 0–7 day, respectively. In gender-specific analyses, the significant association between PM_{10} and female outpatient visits for post-adolescent acne was observed from lag 0 to lag 6 and from 0–1 to lag 0–7, but no significant association was found for males, suggesting that females were more susceptible than males. The results of Z-test also showed that the association of PM_{10} was stronger in females than in males at lag 0–6 and lag 0–7 (Table S1). For NO_2, the significant positive association was evidenced in both males and females. As for SO_2, the significant positive association was only observed at lag 1 for males and at lag 0–7 for females. Thus, PM_{10}, SO_2 and NO_2 concentrations were positively associated with the outpatient visits for post-adolescent acne, and the estimate effects of PM_{10} were stronger in females.

Figure 3 illustrates the exposure–response curves between air pollutants and outpatient-visits for post-adolescent acne at lag 0–7 day. The relationships of both PM_{10} and NO_2 were inverse S-shaped in the curves. Specifically, the association of PM_{10} was linear when the concentrations were above 200 μg/m^3 or below 100 μg/m^3, with no observed lower- and upper-bounds. Interestingly, the relationship turned to be flat when PM_{10} levels ranged from 100 μg/m^3 to 200 μg/m^3. For NO_2, the linear relationship was observed when the concentrations were above 70 μg/m^3 or below 40 μg/m^3, with no observed lower- and upper-bounds. The relationship turned to be flatter when the its levels ranged from 40 μg/m^3 to 70 μg/m^3. Compared with those of PM_{10} and NO_2, the exposure–response curve of SO_2 rose steadily in the entire range of pollutant concentrations, demonstrating its mild but still positive correlation with the risk of post-adolescent acne.

Table 2 reveals the effects of two-pollutant models (lag 0–7). After adjusting for PM_{10} or NO_2, the effect of SO_2 turned to be statistically insignificant. Moreover, the effect of NO_2 remained robust and statistically significant after adjusting for SO_2 (3.75%, 95% CI: 1.25%, 6.25%), but it turned to be insignificant after adjusting for PM_{10} (0.90%, 95% CI: −1.38%, 3.19%). Furthermore, the effect of PM_{10}

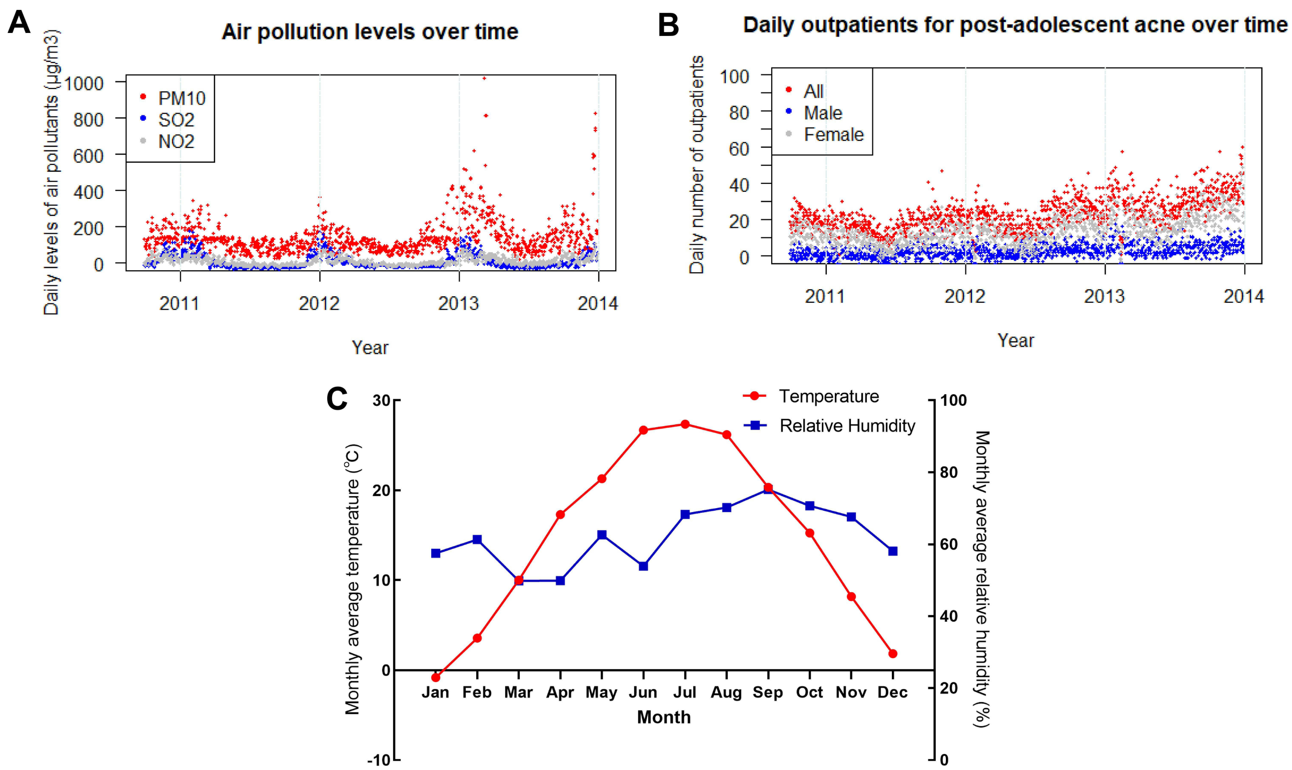

Figure 1 Original plots of outpatients, AP, and meteorological factors over time. (**A** and **B**) shows the daily levels of PM_{10}, SO_2, and NO_2, and the daily outpatient numbers for post-adolescent acne, respectively. (**C**) shows the monthly average temperature and relative humidity during the study period.

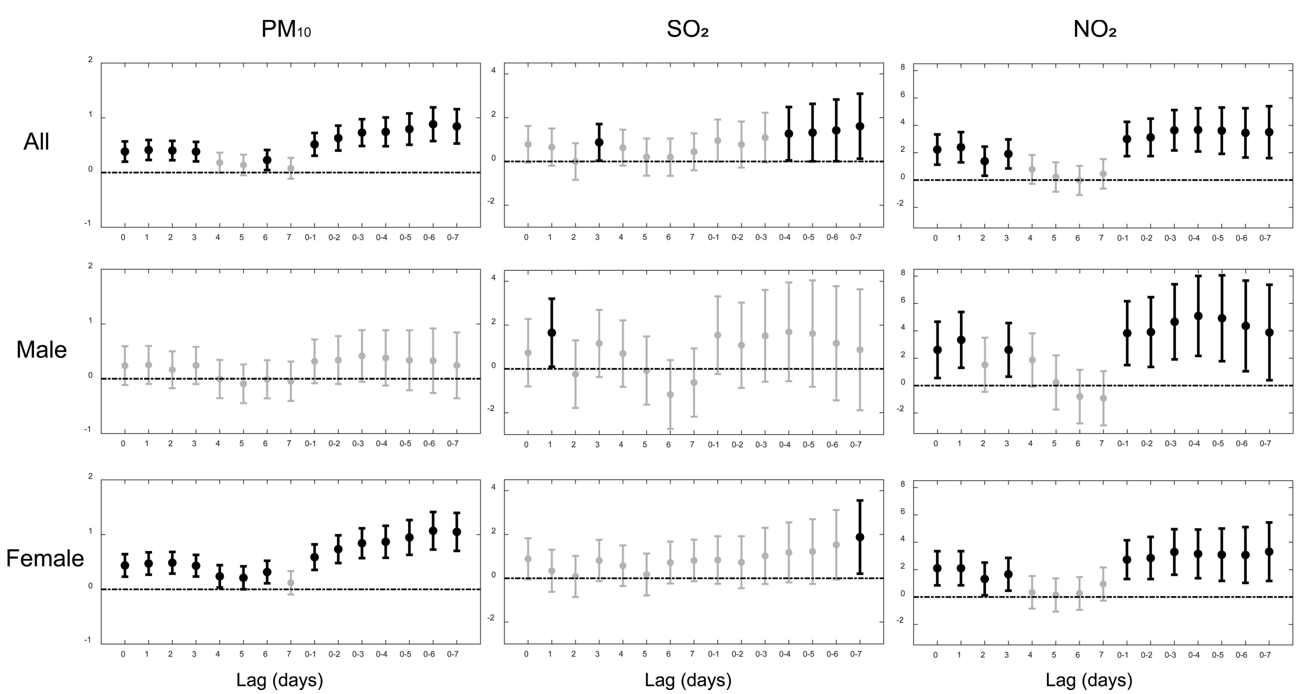

Figure 2 Percent change (mean and 95% CI) of daily outpatient visits for post-adolescent acne associated with per 10 μg/m^3 increase of pollutant concentrations at different lag days in different sex models.

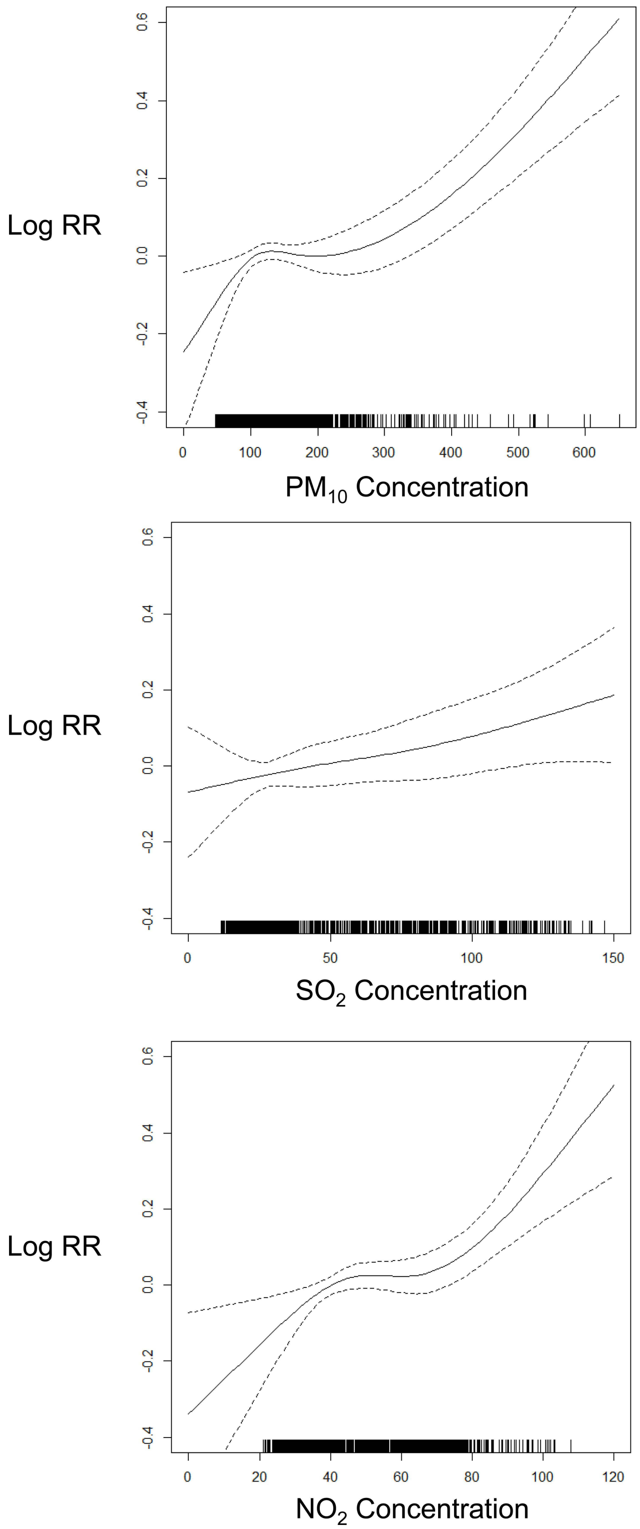

Figure 3 Exposure–response curves for air pollutants and post-adolescent acne. The X-axis is the pollutants' concentrations (μg/m^3) at lag 0–7 day. The Y-axis is the log-relative risk of outpatient visits for post-adolescent acne with per 10 μg/m^3 increase in pollutant concentration. The solid lines show the estimated mean percentages of change in daily outpatient visits for post-adolescent acne. The dotted lines represent the point-wise standard errors, which means 95% confidence intervals.

Table 2 Percent Change (Mean and 95% CI) of Daily Outpatient Visits for Post-Adolescent Acne Associated with per 10 μg/m^3 Increase of Pollutant Concentration at Lag 0–7 Day in Two-Pollutant Models

	Two-Pollutant Models	Estimates
PM_{10}	-	0.84 (0.53, 1.16) *
	+SO_2	0.86 (0.51, 1.21) *
	+NO_2	0.76 (0.38, 1.14) *
SO_2	-	1.61 (0.12, 3.10) *
	+PM_{10}	−0.18 (−1.82, 1.47)
	+NO_2	−0.30(−2.26, 1.65)
NO_2	-	3.50 (1.60, 5.40) *
	+PM_{10}	0.90 (−1.38, 3.19)
	+SO_2	3.75 (1.25, 6.25) *

Note: *P<0.05.
Abbreviations: PM_{10}, particulate matter with an aerodynamic diameter less than 10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide.

increased slightly after adjusting for SO_2 (0.86%, 95% CI: 0.51%, 1.21%), while its effect mildly decreased but still obvious after adjusting for NO_2 (0.76%, 95% CI: 0.38%, 1.14%).

Discussion

In this study, we provided novel evidence of the relationship between short-term AP exposure and outpatient visits for post-adolescent acne. Through time-series analyses, we found positive associations between outpatient visits for post-adolescent acne and short-term exposure to ambient PM_{10}, SO_2, and NO_2. In gender subgroup analyses, the associations of PM_{10} appeared to be more significant in females than in males.

Although acne is typically recognized as an adolescent disorder, a series of studies have reported that the incidence of acne in adults over 25 years old has steadily grown over time.[2,33,34] A consistent rise in the outpatient visits for post-adolescent acne also has been found in Xi'an, China during the study period. The reason for such growth was complex and might be attributed to that some lifestyle factors associated with post-adolescent acne such as smoking[35] and western diet[36,37] are gradually prevalent in adults.[38,39] However, the outpatient visits for post-adolescent acne exhibited a season variation, peaking in winter and decreasing in summer. Such variation indicated that some factors vary with seasonal fluctuation, such as environmental factors, may also affect the incidence and the aggravation of post-adolescent acne. Especially, in the present study, the levels of air pollutants (PM_{10}, SO_2, NO_2) also showed season variations, which seem to have the same fluctuations with the outpatient visits for post-adolescent acne. Therefore, it's imperative to investigate the association between post-adolescent acne and ambient AP.

Our study observed an obvious relationship between short-term exposures to PM_{10}, SO_2, and NO_2 and outpatient visits for post-adolescent acne, which was consistent with previous studies investigating the associations between AP and some inflammatory skin diseases. For example, Guo et al[40] suggested that short-term exposure to AP, represented by PM, was significantly related to the outpatient visits for eczema and dermatitis. Li et al[41] found that short-term elevations of PM_{10}, SO_2, and NO_2 were associated with the increased outpatient visits for eczema. Moreover, Kim et al[42] also indicated that the risk of atopic dermatitis symptoms in young children could be increased with short-term exposure to PM_{10}, NO_2, and ozone (O_3). Such correlations were plausible from a biological perspective: skin, a barrier between internal and external environment, directly contacts air pollutants. Various airborne pollutants can permeate the epidermal barrier, and then trigger skin barrier dysfunction,[43] immune dysregulation,[44] and dermal inflammation.[45] In such processes, the induction of inflammatory cascade, generation of free radicals, activation of AhR (aryl hydrocarbon receptor), and alterations of cutaneous microflora resulted from air pollutants all may be involved in the inflammatory processes and immune responses of post-adolescent acne.[46,47]

Furthermore, our data showed that the association between post-adolescent acne outpatient visits and PM_{10} was more evident in females than in males. One possible explanation was that exposure to PM could result in the imbalance of female hormones via interfering with estrogen-regulated pathways.[48,49] Given that the severity of female acne could fluctuate with hormones in their lifespan, especially in the period of menstruation, pregnancy, and menopause, the irregular changes of hormones affected by AP, especially PM, may further enhance the possibility of the onset and aggravation of post-adolescent acne during female adulthood.[3,50] This can also, at least partly, explain why post-adolescent acne is more prevalent in females than in males.[34,51] In another perspective, males and females have physiological, chemical, and biophysical differences in skin.[52] Such gender difference of skin characteristics in terms of stratum corneum hydration, transepidermal water loss, sebum production, and skin thickness may contribute to their dissimilar abilities against environmental stressors, including AP. From this viewpoint, this study indicated that male skin seems to have stronger properties to counteract or prevent against AP-induced skin damages.

Although it is unavoidable for skin to exposure to air pollutants, many anti-pollutant strategies can be taken into consideration to decrease the risk of post-adolescent acne. To begin with, moisturizer can be utilized to accelerate the recovery of skin barrier and prevent contaminants from adhering directly to the skin.[53] Furthermore, oral or topical antioxidants such as vitamin E,[54] and anti-inflammatory drugs such as adapalene and benzoyl peroxide can be conducive to relieve pollution-induced skin oxidation and inflammation.[55] Lastly, governments should make specific policies to control AP and to reduce the exposure levels of air pollutants.[56–59]

This study has several major advantages. Firstly, this study was conducted with a large sample of post-adolescent acne outpatients. Secondly, we provided the first evidence that short-term exposure to AP may contribute to the increased risk of post-adolescent acne. Thirdly, this research was conducted in Xi'an, a major metropolis in northwestern China with a considerably large population and relatively heavy pollution.

Nonetheless, this study has several limitations. Firstly, like other similar ecological studies, air pollutant levels from fixed site monitoring stations instead of individual exposure levels were included into the main analysis models, which can lead to exposure errors known as "ecological fallacy". Secondly, the data of other pollutants were not available, including particulate matter less than 2.5 µm in aerodynamic diameter ($PM_{2.5}$), O_3, and carbon monoxide (CO). Thirdly, also owing to the limitation of the availability, more confounders which may have potential effects on the relationship between AP and post-adolescent acne were not included for analyses, such as stress status, body mass index, and drug history.[60,61] Fourthly, our data were only collected from a single hospital, which may make our results less representative of the whole city. Therefore, more work is needed to confirm our results in the future.

Conclusions

In conclusion, short-term air pollution (PM_{10}, SO_2, and NO_2) exposure was associated with the increased risk of outpatient visits for post-adolescent acne. More interestingly, females were more sensitive to PM_{10} than men. This study provided novel evidence regarding the relationship between short-term ambient AP exposure and post-adolescence acne, which may have an important bearing on the intervention and prevention of this disease.

Abbreviation

AP, air pollution; CO, carbon monoxide; DOW, day of the week; df, degree of freedom; GAM, generalized additive model; NO_2, nitrogen dioxide; O_3, ozone; PACF, partial autocorrelation function; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter; $PM_{2.5}$, particulate matter less than 2.5 μm in aerodynamic diameter; SO_2, sulfur dioxide.

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Disclosure

No potential conflict of interest was reported by the authors.

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