Letter to the Editor

Retrospective Study of Effect of Fine Particulate Matter on Acute Exacerbation of Patients with Idiopathic Pulmonary Fibrosis*

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Acute exacerbation of idiopathic pulmonary fibrosis (AEIPF) is the most important cause of health deterioration and death as a result of idiopathic pulmonary fibrosis (IPF). In recent years, the hospitalization and mortality rates due to AEIPF have increased significantly[1]. However, until the present, the cause of AEIPF remains unclear, thereby needing research attention. The harm of long-term sustained exposure or short-term acute exposure to air pollutants to respiratory health has been confirmed by a large number of studies[2-3]. Current studies have suggested that the incidence and progression of IPF are related to continuous exposure to atmospheric fine particles[4]. However, few reports are available on the acute aggravation of IPF induced by atmospheric fine particulate matter. In our clinical work in recent years, we found that the hospitalization time of AEIPF patients was related to the occurrence of local air pollution, and the number of hospitalized patients increased significantly during the period of severe air pollution. Thus, we adopted a retrospective analysis of AEIPF patients clinical data from January 2005 to December 2017 (a total of 13 years) in the first affiliated hospital of Harbin Medical University. We further analyzed the correlation between patients' hospitalization time and atmospheric pollutants to study the effect of air pollutants on the exacerbation of IPF in adults and the characteristics of the affected population.

We screened the hospitalized cases diagnosed as AEIPF in the respiratory department of the hospital. The following were the inclusion criteria: the results of lung HRCT images of patients should be in line with the IPF diagnostic criteria formulated by ATS/ERS in 2011[5] and the AE-IPF diagnostic criteria in 2015[6]. Cases of interstitial pulmonary disease of other causes were excluded. A total of 811 patients were selected, including 327 males and 484 females, with an average age of 64 ± 5.3 years.

Relevant information on air pollution is provided by the School of Environment, Harbin University of Technology. The information provided includes monitoring data on air pollutant composition, and various particle types and concentrations in Heilongjiang from January 2013 to December 2017. In accordance with the environmental air quality standard (GB 3095-2012), the limit of $PM_{2.5}$ 24-h average daily concentration ranges from 0–35 g/m^3 as level 1 and 35–75 g/m^3 as level 2. The annual average $PM_{2.5}$ concentration limit of 0–15 g/m^3 is level 1 and 15–35 g/m^3 is level 2[7]. Combined with the local climate characteristics, January, February, October, November, and December of each year were determined as the serious period of air pollution. The AEIPF patients hospitalized during this period were identified as the high concentration group for inhaled fine particles (group A) and the patients hospitalized during the rest of the months were the low concentration group (group B).

We used SPSS16.0 software to conduct statistical analysis and research on the clinical data of patients and atmospheric environment monitoring data. The analysis results are as follows. The ratio of AEIPF inpatients to the total number of inpatients in the respiratory department from January 2005 to December 2017 is shown in Figure 1, indicating that the ratio of AEIPF inpatients increased in 13 years. The ratio of AEIPF to inpatients has increased

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significantly since 2012, and 2013 is the year with the highest ratio ($P < 0.05$).

According to the monitoring data of air pollutants in Harbin, the correlation between the concentration of different components of air pollutants and the hospitalization rate of AEIPF from January 2013 to December 2017 was further analyzed. The results are shown in Table 1. As the table indicates, the correlation coefficient *OR* value between the hospitalization rate of AEIPF and the concentration of PM_{10}, $PM_{2.5}$, and SO_2 in the atmosphere is 0.862, 0.886, and 0.761, respectively, with a positive correlation. The *OR* values of CO and O_3 were –0.371 and –0.525, respectively, showing a negative correlation. The hospital admission rate decreased with the decrease of pollutant concentration in 2017, which further confirmed the existence of a positive correlation between the concentration of different components of air pollutants and the hospitalization rate of AEIPF.

As this region is located in the cold temperate zone, the cold climate and low air pressure in winter are not conducive to the diffusion of pollutants. Winter heating time is long, thereby aggravating the slow release of air pollutants and other adverse factors. In this regard, we analyzed the relationship between the concentration of $PM_{2.5}$ in the atmosphere and the hospitalization rate of AEIPF in different months from 2013 to 2017. The correlation rates were *OR* = 0.599 ($P = 0.039$), *OR* = 0.756 ($P = 0.005$), *OR* = 0.772 ($P = 0.003$), *OR* = 0.771 ($P = 0.003$), and *OR* = 0.564 ($P = 0.056$). The results of statistical analysis are shown in Supplementary Table S1 and Figure S1 (available in www.besjournal.com). The results of *OR* value indicate a significant positive correlation between $PM_{2.5}$ concentration and inpatient ratio in different months of each year. Thus, $PM_{2.5}$ concentration may be an important risk factor for acute aggravation of IPF hospitalization.

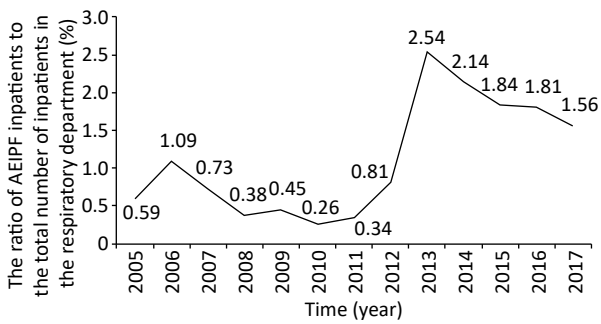

Figure 1. Trend chart of ratio of AEIPF inpatients to total inpatients in respiratory department over time.The *Chi-square* value of the linear trend is 141.163, $P < 0.0001$.

To identify susceptible populations affected by atmospheric fine particulate matter, we further analyzed the clinical characteristics of 811 patients with AEIPF. The results showed that in the period of high atmospheric pollutant concentration (group A), female AEIPF inpatients accounted for 67.07% of the hospitalized patients, higher than the figure for male patients ($P < 0.05$). The hospitalization ratio of patients aged over 65 years during the same period was 59.23%, higher than that of the two other groups ($P < 0.05$). The inpatient ratio of the smoking group was 61.43%, higher than that of the non-smoking group ($P < 0.05$). The increased $PM_{2.5}$ concentration has a greater impact on AEIPF patients who are female, over 65 years old, and smoking. The results are shown in Table 2.

We have consulted the literature on the effect of fine particulate matter on the human body, and found that the effect on women is relatively obvious[8], which is consistent with our research conclusion. However, the reasons for the occurrence need to be clarified. In terms of the influence of smoking, the reasons may be that long-term smoking destroys the defense function of the airway mucosa and directly causes damage on the airway mucosa epithelium, thereby increasing the sensitivity to the damage induced by particulate matter. Several

Table 1. Correlation analysis of annual hospitalization rate of AEIPF and concentration of various components of air pollutants from 2013 to 2017

Items	2013	2014	2015	2016	2017	*OR* value
Rate of AEIPF inpatient (%) (n = 811)	18.740	17.020	15.660	14.920	13.560	
PM_{10} (mg/m^3)	0.119	0.111	0.103	0.074	0.085	0.862
SO_2 (mg/m^3)	0.044	0.057	0.040	0.029	0.025	0.761
$PM_{2.5}$ (mg/m^3)	0.081	0.072	0.070	0.051	0.057	0.886
CO (mg/m^3)	1.029	0.890	1.800	2.000	1.056	–0.371
O_3 (mg/m^3)	0.038	0.042	0.106	0.106	0.059	–0.525

Table 2. Comparison of clinical features among different groups

Patient characteristics	Total number (%)	Group A (%)	Group B (%)	*Chi*-square value	*F*
Sex					
Male	327 (40.32)	189 (32.93)	138 (58.23)	44.624	< 0.0001
Female	484 (59.68)	385 (67.07)	99 (41.77)		
Age (years)					
< 40	17 (2.10)	10 (1.74)	7 (2.95)	12.169	0.0005
40–65	345 (42.54)	224 (39.02)	121 (51.05)		
> 65	449 (55.36)	340 (59.23)	109 (45.99)		
Smoke					
Yes	424 (52.35)	352 (61.43)	72 (30.38)	64.803	< 0.0001
No	386 (47.65)	221 (38.57)	165 (69.62)		

reports indicate that under the effect of fine particles, the smoking population shows a more serious rate of lung function decline and inflammatory response than the non-smoking population[9-10]. This result confirms the reliability of our research conclusions.

The authors declare no conflict of interest.

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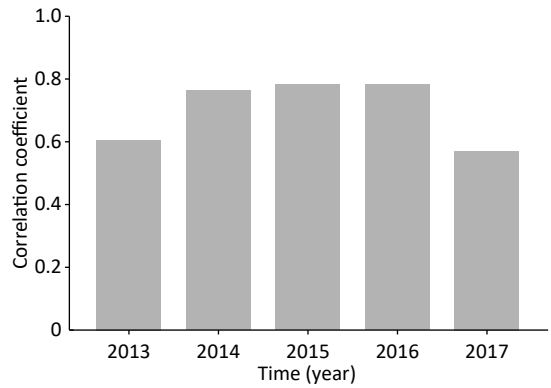
Supplementary Table S1. Correlation analysis of AEIPF rate and $PM_{2.5}$ concentration in different months of each year

Month	2013 (*n* = 152)		2014 (*n* = 138)		2015 (*n* = 127)		2016 (*n* = 121)		2017 (*n* = 110)	
	AEIPF ratio	$PM_{2.5}$ concentrations	AEIPF ratio	$PM_{2.5}$ concentrations	AEIPF ratio	$PM_{2.5}$ concentrations	AEIPF ratio	$PM_{2.5}$ concentrations	AEIPF ratio	$PM_{2.5}$ concentrations
Jan.	13.2	189.46	15.2	124.61	15.7	120.97	14.9	96.16	14.5	121.98
Feb.	10.5	88.22	13.0	116.38	11.8	115.86	11.6	66.62	7.3	72.55
Mar.	6.6	48.48	4.3	58.57	4.7	64.19	8.3	55.16	9.1	55.16
Apr.	3.9	44.81	5.1	49.80	2.4	53.03	3.3	39.97	4.5	63.85
May.	3.3	40.87	3.6	27.88	3.1	28.81	4.1	27.35	2.7	30.13
Jun.	3.3	42.85	2.9	29.70	3.9	35.00	1.7	24.32	3.6	23.81
Jul.	3.3	23.52	3.6	48.81	3.1	33.65	3.3	24.30	2.7	24.30
Aug.	10.5	33.39	9.4	28.59	11.0	24.26	12.4	23.15	8.2	15.72
Sep.	7.9	30.53	5.1	22.49	8.7	22.20	7.4	23.49	11.8	20.20
Oct.	3.9	142.16	8.7	157.83	4.7	56.71	3.3	43.78	7.3	92.22
Nov.	14.5	90.39	14.5	145.14	13.4	149.43	13.2	97.55	12.7	96.65
Dec.	19.1	155.14	14.5	98.80	17.3	145.06	16.5	91.31	15.5	73.34
OR	0.599		0.756		0.772		0.771		0.564	
P values	0.039		0.005		0.003		0.003		0.056	

***Note*.** The unit of AEIPF rate is % and the unit of $PM_{2.5}$ concentration is $\mu g/m^3$.



Supplementary Figure S1. Correlation analysis of AEIPF hospitalization rate and $PM_{2.5}$ concentration in different months of each year.