



## Short-term effects of the chemical components of fine particulate matter on pulmonary function: A repeated panel study among adolescents



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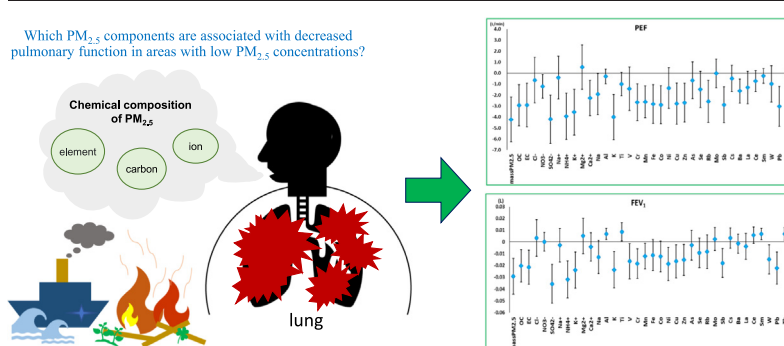
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### HIGHLIGHTS

- Concentrations of PM<sub>2.5</sub> chemical components vary depending on the season.
- Effects on pulmonary function vary based on the type of PM<sub>2.5</sub> component.
- Pulmonary function declined significantly with enhanced levels of several components.
- Sulfate exerted the greatest effect on pulmonary function among the PM<sub>2.5</sub> components.
- The effects of many PM<sub>2.5</sub> components were stronger in the fall than in the spring.

### GRAPHICAL ABSTRACT



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### ABSTRACT

The effects of the chemical components of fine particulate matter (PM<sub>2.5</sub>) have been drawing attention. However, information regarding the impact of low PM<sub>2.5</sub> concentrations is limited. Hence, we aimed to investigate the short-term effects of the chemical components of PM<sub>2.5</sub> on pulmonary function and their seasonal differences in healthy adolescents living on an isolated island without major artificial sources of air pollution. A panel study was repeatedly conducted twice a year for one month every spring and fall from October 2014 to November 2016 on an isolated island in the Seto Inland Sea, which has no major artificial sources of air pollution. Daily measurements of peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV<sub>1</sub>) were performed in 47 healthy college students, and the concentrations of 35 chemical components of PM<sub>2.5</sub> were analyzed every 24 h. Using a mixed-effects model, the relationship between pulmonary function values and concentrations of PM<sub>2.5</sub> components was analyzed. Significant associations were observed between several PM<sub>2.5</sub> components and decreased pulmonary function. Among the ionic components, sulfate was strongly related to decreases in PEF and FEV<sub>1</sub> (−4.20 L/min [95 % confidence interval (CI): −6.40 to −2.00] and −0.04 L [95 % CI: −0.05 to −0.02] per interquartile range increase, respectively). Among the elemental components, potassium induced the greatest reduction in PEF and FEV<sub>1</sub>. Therefore, PEF and FEV<sub>1</sub> were significantly reduced as the concentrations of several PM<sub>2.5</sub> components increased during fall, with minimal changes observed during spring. Several chemical

**Abbreviations:** CI, confidence interval; EC, elemental carbon; FEV<sub>1</sub>, forced expiratory volume in 1 s; IQR, interquartile range; OC, organic carbon; PEF, peak expiratory flow; PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter of ≤2.5 μm.

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components of PM<sub>2.5</sub> were significantly associated with decreased pulmonary function among healthy adolescents. The concentrations of PM<sub>2.5</sub> chemical components differed by season, suggesting the occurrence of distinct effects on the respiratory system depending on the type of component.

## 1. Introduction

Various studies have evaluated the effects of airborne fine particulate matter with an aerodynamic diameter of  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) on human health (Kampa and Castanas, 2008; Feng et al., 2016; Strassmann et al., 2021; Gehring et al., 2013). The impact of PM<sub>2.5</sub> on the respiratory system is widely established worldwide (Rice et al., 2016; Li et al., 2018; Kariisa et al., 2015; U.S. Environmental Protection Agency, 2022). Ambient PM<sub>2.5</sub> comprises various chemical components, including carbons, ionic species, and metallic elements (Frank and Julia, 2012; Behera and Sharma, 2010; Adams et al., 2015; Buczynska et al., 2014) derived from diverse sources, varying by region and season. Recent studies have focused on examining the relationship between the composition of PM<sub>2.5</sub> and its impact on human health (Roemer et al., 2000; Guo et al., 2022). A previous panel study showed that the water-soluble ions in PM<sub>2.5</sub> and some metals can exert short-term effects on the cardiopulmonary function of patients with chronic obstructive pulmonary disease (COPD) (Zhou et al., 2021). In addition, the ionic components of PM<sub>2.5</sub> can enhance airway inflammation (Shi et al., 2016), while the concentrations of certain components, such as elemental carbon (EC) in PM<sub>2.5</sub>, could increase the number of hospitalizations due to ischemic stroke (Wang et al., 2019). Moreover, the PM<sub>2.5</sub> components can affect the expression of stress hormones (Niu et al., 2018) and blood biomarkers (Wu et al., 2016; Liu et al., 2017).

To date, epidemiological studies have predominantly focused on investigating areas with relatively high PM<sub>2.5</sub> concentrations. In 2021, the World Health Organization revised the air quality guidelines and recommended 5 and  $\leq 15 \mu\text{g}/\text{m}^3$  as the annual and daily average concentrations of PM<sub>2.5</sub>, respectively (World Health Organization, 2021). However, the effect of low concentrations of ambient PM<sub>2.5</sub> on the respiratory system remains unexplored. Furthermore, little is known regarding the PM<sub>2.5</sub> exposure levels of healthy adolescents while performing daily living activities. We have previously reported that the mass concentrations of PM<sub>2.5</sub> were associated with reduced pulmonary function, especially during fall season (Yoda et al., 2019); however, the association between the concentration of PM<sub>2.5</sub> components and the potential respiratory effects needs to be comprehensively clarified. In addition, the seasonal variations in the effects of chemical components of PM<sub>2.5</sub> on the respiratory system need to be clarified, given that, in addition to the PM<sub>2.5</sub> mass concentration, the PM<sub>2.5</sub> component concentration may differ depending on the season (Ito et al., 2011; Zhou et al., 2022).

Previously, we conducted a panel study of the same group of healthy adolescents twice a year (1 month each time) every spring and fall for over 3 years and reported the short-term effects of exposure to PM<sub>2.5</sub> mass concentrations on pulmonary function (Yoda et al., 2017; Yoda et al., 2019). In the present study, we aimed to clarify the relationship between the concentration of PM<sub>2.5</sub> chemical components and pulmonary function among adolescents and to determine the seasonal differences in the effects of chemical components. We analyzed the results of the repeated panel study five times during the spring and fall seasons within two and a half years.

## 2. Methods

### 2.1. Survey protocol and participants

This study was part of a 3-year epidemiological study that investigated the effects of PM<sub>2.5</sub> and ozone on respiratory health in areas with different air pollution levels. A panel study was repeatedly conducted to elucidate the short-term effects of PM<sub>2.5</sub> components on the pulmonary function of healthy adolescents (1 month each time) every spring and fall from October

2014 to November 2016. The investigation was performed on Yuge Island, Ehime Prefecture, an isolated island in the Seto Inland Sea, western Japan. This island has a mild climate and no major sources of artificial air pollution in the surrounding area. Although the automobile traffic volume is low on the island, the concentrations of PM<sub>2.5</sub> are relatively high due to marine traffic in the surrounding area. The details of the study conducted have been published previously (Yoda et al., 2017; Yoda et al., 2019). Briefly, students living on the island who belonged to a single class in the College of Technology were recruited in October 2014. Forty-three students (29 male students and 14 female students) participated in the first study. During the study period, some participants were replaced due to transfers, dropouts, or new participation. Finally, total of 47 students (aged 16–20 years; 31 male students and 16 female students) participated in each of the studies. In each study period, the pulmonary function test was solely performed by each participant every morning, and the PM<sub>2.5</sub> was collected every 24 h to measure the concentration of its components. This study was approved by the Ethics Review Board of Hyogo Medical University. Written informed consent was provided by all participants prior to the initiation of the study.

### 2.2. Pulmonary function tests

Pulmonary function tests were performed using an electronic peak flow meter (Vitalograph 2110, Vitalograph Ltd., Buckingham, UK), which was provided to each enrolled student. Self-measurements of peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV<sub>1</sub>) were performed at 8:30 to 9:00 every morning from Monday through Friday for approximately one month in each study period. Self-measurement was performed in a standing position in accordance with the American Thoracic Society (ATS) guidelines (Miller et al., 2005) prior to the start of the survey. Peak flow meters were calibrated using a 3-L syringe (Hans Rudolph, Inc., KS, USA) before each test period. The height and weight of each participant were measured prior to each test period. The health status and medical history of the participants were evaluated using a standard questionnaire (Ferris, 1978) prior to the initiation of this study.

### 2.3. Environmental measurements

To measure the concentration of the PM<sub>2.5</sub> components, a PM<sub>2.5</sub> low-volume air sampler (Thermo Model 2025i Sequential Air Sampler, Thermo Fisher Scientific, Massachusetts, USA) was installed on the rooftop of the school building in accordance with the United States Federal Reference Method (US Environmental Protection Agency, 2016). The air was continuously aspirated at a flow rate of 16.7 L/min and collected every morning at 24-h intervals from 10:00 am to 10:00 am the following morning. Polytetrafluoroethylene (PTFE) filters (47 mm  $\phi$ ; Whatman 7592–104, Cytiva, Tokyo, Japan) and quartz fiber filter paper (47 mm  $\phi$ ; Pallflex 2500 QAT-UP, Pall Corporation, Washington, NY, USA) were used for sampling. The quartz fiber filter paper was heated in an electric furnace at 350 °C for 1 h before use. The particles were collected on PTFE filter paper, and the mass concentration was measured using an electron ultra-micro balance (SE 2-F, readability: 0.1  $\mu\text{g}$ ; Sartorius, Göttingen, Germany). The organic carbon (OC) and EC were collected using a quartz fiber filter paper and analyzed using a thermal separation optical correction method (OCEC Lab analyzer, Sunset Laboratory Co., Ltd). For the ionic components, the concentrations of chloride (Cl<sup>-</sup>), nitrate (NO<sub>3</sub><sup>-</sup>), sulfate (SO<sub>4</sub><sup>2-</sup>), sodium (Na<sup>+</sup>), ammonium (NH<sub>4</sub><sup>+</sup>), potassium (K<sup>+</sup>), magnesium (Mg<sup>2+</sup>), and calcium (Ca<sup>2+</sup>) were measured using ion chromatography (ICS-2100, Thermo Fisher Scientific, Massachusetts, USA). For the elemental components, the

concentrations of sodium (Na), aluminum (Al), potassium (K), calcium (Ca), scandium (Sc), titanium (Ti), vanadium (V), chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), arsenic (As), selenium (Se), rubidium (Rb), molybdenum (Mo), antimony (Sb), cesium (Cs), barium (Ba), lanthanum (La), cerium (Ce), samarium (Sm), hafnium (Hf), tungsten (W), tantalum (Ta), thorium (Th), and lead (Pb) were measured using inductively coupled plasma mass spectrometry (SERIES II, Thermo Fisher Scientific, Massachusetts, USA).

#### 2.4. Statistical analysis

A mixed effects model was employed to determine the relationship between the pulmonary function measurements and the 24-h average concentrations of PM<sub>2.5</sub> mass, carbon, ionic, and elemental components measured from 10:00 am of the day before the examination. This model takes into account the fixed and random effects and is suitable for analyzing serially correlated data by individual repeated measurements (Molenberghs and Verbeke, 2001). The estimated changes in PEF and FEV<sub>1</sub> for every increase in the interquartile range (IQR) of each component concentration were determined along with their 95 % confidence intervals (CIs), after controlling for age, height, temperature, and humidity. The daily atmospheric temperature and relative humidity values were collected from a monitoring station near the island. To evaluate the seasonal effects of PM<sub>2.5</sub> components, the relationship between the concentration of each component and the pulmonary function results was analyzed using data collected from 2015 to 2016, in which the PM<sub>2.5</sub> concentrations were obtained in spring and fall.

All statistical analyses were performed using SPSS 24.0 (IBM Corp., Armonk, NY, USA), and a *p*-value of <0.05 was considered significant.

### 3. Results

#### 3.1. Descriptive statistics

Table 1 shows the participants' baseline characteristics. A total of 47 participants (31 male students and 16 female students) participated in at least one of the five surveys. Overall, 4155 pulmonary function tests were performed during the study period. The mean ( $\pm$  standard deviation) values of PEF and FEV<sub>1</sub> in male participants were 448.5  $\pm$  114.6 L/min and 2.48  $\pm$  0.60 L, respectively, while those in female participants were 340.7  $\pm$  56.0 L/min and 1.82  $\pm$  0.39 L, respectively.

Table 2 presents the daily concentrations of PM<sub>2.5</sub> mass and components recorded during the study period. The average mass concentration of PM<sub>2.5</sub> was 14.9  $\mu$ g/m<sup>3</sup>. The carbon components (OC and EC) accounted for 27.9 % of the PM<sub>2.5</sub> mass concentration. Among the ionic components, SO<sub>4</sub><sup>2-</sup> composed the highest proportion of the PM<sub>2.5</sub> mass concentration (31 %), followed by NH<sub>4</sub><sup>+</sup> (11.6 %) and NO<sub>3</sub><sup>-</sup> (3.1 %). Of the 29 elements, Sc, Ta, Ca, and Hf were excluded from the analysis, as >60 % of the concentrations were below the lower limits of detection. Among the elemental components, the percentage of Fe in PM<sub>2.5</sub> was the highest (1.3 %), followed by those of K and Na (1.0 and 0.7 %, respectively). Table S1 presents the correlation coefficients of the concentrations of mass, 8 ions, and 25 elemental

**Table 1**

Baseline characteristics of the study participants (mean  $\pm$  SD).

	Male (n = 31)		Female (n = 16)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Age (years)	16.3 $\pm$ 0.9	16–20	16.2 $\pm$ 0.9	15–19
Height (cm)	167.6 $\pm$ 6.5	154.4–177.9	157.2 $\pm$ 4.9	147.2–166.9
PEF (L/min)	448.5 $\pm$ 114.6	86–834	340.7 $\pm$ 56.0	125–575
FEV <sub>1</sub> (L)	2.48 $\pm$ 0.60	0.43–4.55	1.82 $\pm$ 0.39	0.89–3.19
Measurements of pulmonary function (n)	2600		1555	

FEV<sub>1</sub>, forced expiratory volume in 1 s; PEF, peak expiratory flow; SD, standard deviation.

**Table 2**

Descriptive statistics of the daily concentrations of PM<sub>2.5</sub> mass and components during the study period.

	n	Mean	SD	Min	Max	IQR
PM <sub>2.5</sub> , total mass ( $\mu$ g/m <sup>3</sup> )	157	14.9	7.5	2.1	45.8	9.4
Carbons ( $\mu$ g/m <sup>3</sup> )						
OC	157	3.3	1.6	0.67	11	1.9
EC	157	0.83	0.48	0.13	2.5	0.65
Ions ( $\mu$ g/m <sup>3</sup> )						
Cl <sup>-</sup>	157	0.05	0.05	0.003	0.29	0.06
NO <sub>3</sub> <sup>-</sup>	157	0.46	0.56	0.03	4.5	0.35
SO <sub>4</sub> <sup>2-</sup>	157	4.6	3.1	0.63	19	3.9
Na <sup>+</sup>	157	0.12	0.07	0.02	0.45	0.07
NH <sub>4</sub> <sup>+</sup>	157	1.7	1.3	0.13	7.8	1.5
K <sup>+</sup>	157	0.16	0.08	0.03	0.43	0.11
Mg <sup>2+</sup>	157	0.02	0.01	0.005	0.06	0.01
Ca <sup>2+</sup>	157	0.05	0.02	0.01	0.16	0.03
Elements (ng/m <sup>3</sup> )						
Na	157	108	59	25	480	59
Al	157	33.0	41.5	2.4	430	22
K	157	144	75	25	440	103
Ti	157	3.1	2.7	0.23	24	2.2
V	157	5.3	3.9	0.15	22	5.2
Cr	157	1.0	0.6	0.2	3.0	0.74
Mn	157	12.9	8.5	1.2	50	9.8
Fe	157	192	114	12	570	164
Co	157	0.05	0.03	0.004	0.14	0.04
Ni	157	2.0	1.5	0.1	8.9	1.9
Cu	157	2.5	1.5	0.13	8.5	2.0
Zn	157	37	24	4.4	150	30
As	157	2.0	1.4	0.06	6.5	1.7
Se	157	1.5	0.9	0.13	5.7	1.2
Rb	157	0.75	0.51	0.07	2.9	0.62
Mo	157	0.76	0.61	0.04	4.8	0.66
Sb	157	0.80	0.54	0.04	3.7	0.56
Cs	157	0.27	0.31	0.01	3.1	0.28
Ba	157	0.79	0.66	0.07	4.9	0.52
La	157	0.06	0.04	0.002	0.25	0.05
Ce	157	0.05	0.05	0.004	0.43	0.04
Sm	157	0.003	0.003	0.0003	0.032	0.002
W	157	0.19	0.22	0.004	1.6	0.18
Pb	157	12.3	6.9	0.53	38	8.7
Th	157	0.005	0.007	0.0004	0.07	0.004

EC, elemental carbon; IQR, interquartile range; OC, organic carbon; PM<sub>2.5</sub>, particulate matter with diameter  $\leq$  2.5  $\mu$ m; SD, standard deviation.

components in PM<sub>2.5</sub>. The PM<sub>2.5</sub> mass concentrations strongly correlated with OC, EC, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, V, Co, Ni, Zn, As, Sb, Ba, and Ce.

#### 3.2. Estimated effects of mass and chemical components of PM<sub>2.5</sub> on pulmonary function

Fig. 1 shows the estimated changes in PEF and FEV<sub>1</sub> associated with the IQR increases in the daily concentration of PM<sub>2.5</sub> mass and components prior to the pulmonary function measurements. An elevated PM<sub>2.5</sub> mass concentration (IQR: 9.35  $\mu$ g/m<sup>3</sup>) was significantly associated with reduced PEF ( $-4.22$  L/min [95 % CI:  $-6.27$  to  $-2.18$ ]) and FEV<sub>1</sub> ( $-0.03$  L [95 % CI:  $-0.04$  to  $-0.01$ ]) (Fig. 1). Significant associations were also observed between increased concentrations of carbon components (OC and EC) and decreased PEF and FEV<sub>1</sub> values. With regard to the ion components of PM<sub>2.5</sub>, increased SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>, and K<sup>+</sup> concentrations were significantly associated with decreased PEF and FEV<sub>1</sub> values. SO<sub>4</sub><sup>2-</sup> was associated with the largest decrease in pulmonary function per IQR increase, with PEF decreasing by  $-4.20$  L/min [95 % CI:  $-6.40$  to  $-2.00$ ] and FEV<sub>1</sub> by  $-0.04$  L [95 % CI:  $-0.05$  to  $-0.02$ ]. The elevated concentrations of NO<sub>3</sub><sup>-</sup> and Ca<sup>2+</sup> were also significantly associated with decreased PEF but were not associated with decreased FEV<sub>1</sub>.

With regard to the 25 elemental components of PM<sub>2.5</sub>, the increased concentrations of Na, K, Cr, Mn, Fe, Co, Cu, Zn, Rb, Sb, Ba, and Pb were significantly associated with decreased PEF values. K had the largest decrease in PEF per IQR increase ( $-4.01$  L/min [95 % CI:  $-6.07$  to  $-1.94$ ]), followed by Pb ( $-3.03$  L/min [95 % CI:  $-4.84$  to  $-1.22$ ]). Similarly,

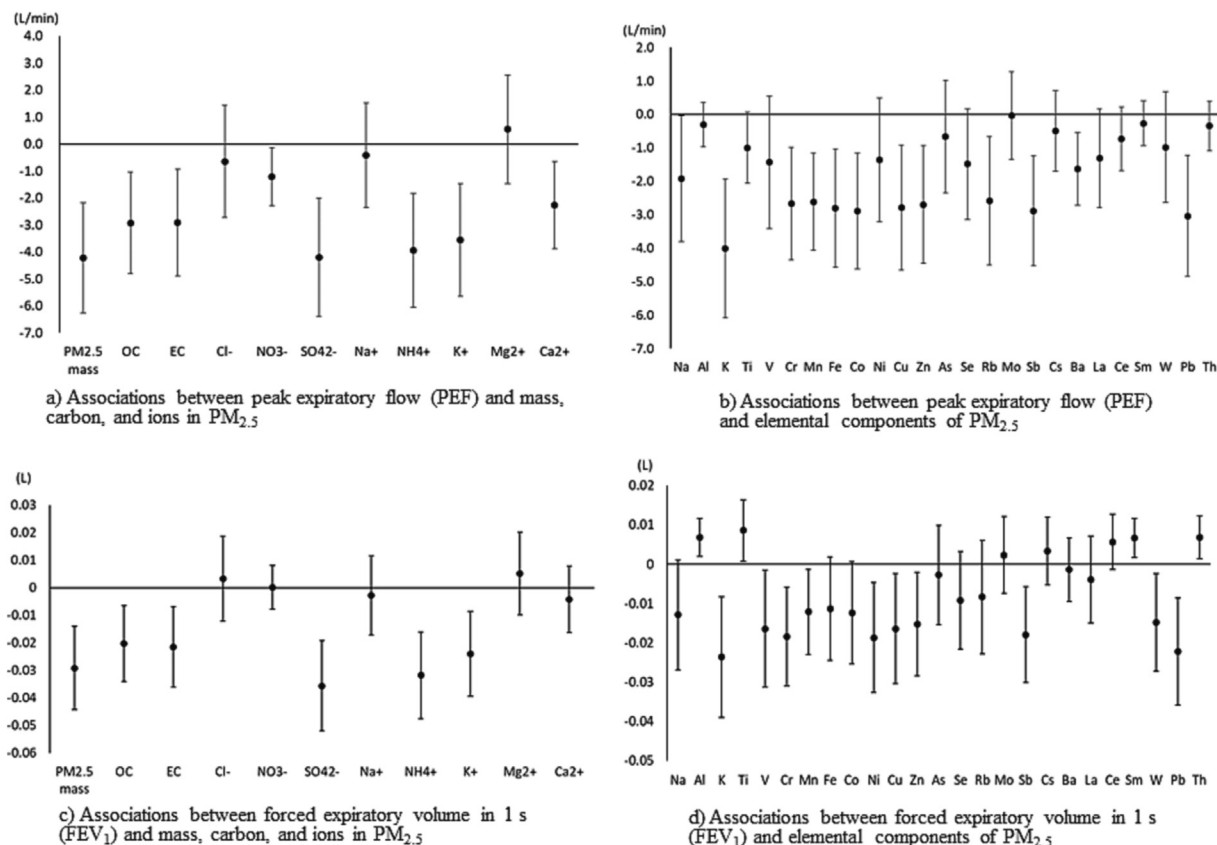


Fig. 1. Estimated changes in the pulmonary function values with increases in the interquartile range of each daily concentration of mass and the chemical components of fine particulate matter (PM<sub>2.5</sub>).

the FEV<sub>1</sub> value significantly decreased as the concentrations of K, V, Cr, Mn, Ni, Cu, Zn, Sb, W, and Pb increased. An IQR increase in the K concentration was associated with the largest decrease in the FEV<sub>1</sub> value (−0.02 L [95 % CI: −0.04 to −0.01]), followed by the Pb concentration.

### 3.3. Comparison of the estimated effects of mass and chemical components of PM<sub>2.5</sub> by season

Next, the seasonal differences in the effects of PM<sub>2.5</sub> chemical components on pulmonary function were examined using the results measured in spring and fall from 2015 to 2016. A total of 46 students participated in the 2-year study period. The pulmonary function tests were conducted approximately 3259 times during this period (1685 times in spring and 1574 times in fall). The mean PM<sub>2.5</sub> mass concentrations during spring and fall were 18.3 and 12.3 μg/m<sup>3</sup>, respectively, showing a higher concentration in spring than that in fall. The concentrations of carbon components were higher in spring than those in fall, while the concentrations of ionic and elemental components differed depending on the season (Table S2). No significant decrease was observed in the PEF value associated with an increased concentration of any PM<sub>2.5</sub> component during spring (Fig. 2A). However, the PEF value was significantly decreased as the concentrations of several components increased during fall (Fig. 2B). During fall, the SO<sub>4</sub><sup>2-</sup> (−4.95 L/min [95 % CI: −8.07 to −1.84]) and Sb (−4.62 L/min [95 % CI: −8.24 to −0.99]) were among the ion and elemental components, respectively, that exhibited the largest changes in PEF per IQR increase. An increase in the Cr concentration during spring was associated with a significant decrease in the FEV<sub>1</sub> value, but its association with other components was not significant (Fig. 3A). During fall, as observed for PEF, the SO<sub>4</sub><sup>2-</sup> showed the largest change in the FEV<sub>1</sub> value per IQR increase among ionic components (−0.05 L [95 % CI: −0.08 to −0.03]). Among the elemental components, the FEV<sub>1</sub> value was significantly decreased as the concentrations of several components increased (Fig. 3B).

## 4. Discussion

The present study evaluated the relationship between chemical components of PM<sub>2.5</sub> and pulmonary function in adolescents living on an isolated island with relatively low PM<sub>2.5</sub> concentrations for two and a half years. We have previously reported (Yoda et al., 2019) that an increased PM<sub>2.5</sub> mass concentration could reduce the PEF and FEV<sub>1</sub> values. In the present study, we identified the short-term effects of several chemical components of PM<sub>2.5</sub> on pulmonary function. SO<sub>4</sub><sup>2-</sup> among the ionic components and K among the elemental components demonstrated the highest drop per IQR increase in each component concentration. The decrease in the FEV<sub>1</sub> value per IQR increase in SO<sub>4</sub><sup>2-</sup> concentration was larger than that in the PM<sub>2.5</sub> mass concentration.

PEF was associated with more substances compared with FEV<sub>1</sub>. This finding differs from that reported by Strak et al. (2012), which showed a significant association between various contaminants and FEV<sub>1</sub>, but no association with PEF in healthy individuals. However, only three to seven pulmonary function tests were performed per person. Conversely, a previous study in Shanghai that examined the relationship between the pulmonary function in patients with COPD and the concentrations of OC, EC, and eight ionic components of PM<sub>2.5</sub> has shown that the morning PEF value was associated with more items than the morning FEV<sub>1</sub> value (Chen et al., 2017).

A study conducted among elementary school children reported a strong association between OC and EC in PM<sub>2.5</sub> and exhaled nitric oxide (FeNO) and inflammatory cytokines (Wu et al., 2021). Huang et al. (2019) reported that the carbonic components of PM<sub>2.5</sub> exert a short-term effect on the pulmonary function of healthy young adults. Among the carbon components of PM<sub>2.5</sub>, OC may be of greater importance as a risk factor for decreased pulmonary function than EC (Hu et al., 2020). Exposure to the carbon components of PM<sub>2.5</sub> causes an inflammatory response in the body and increases the release of inflammatory cytokines (Zhang et al., 2013), which may affect the respiratory system.



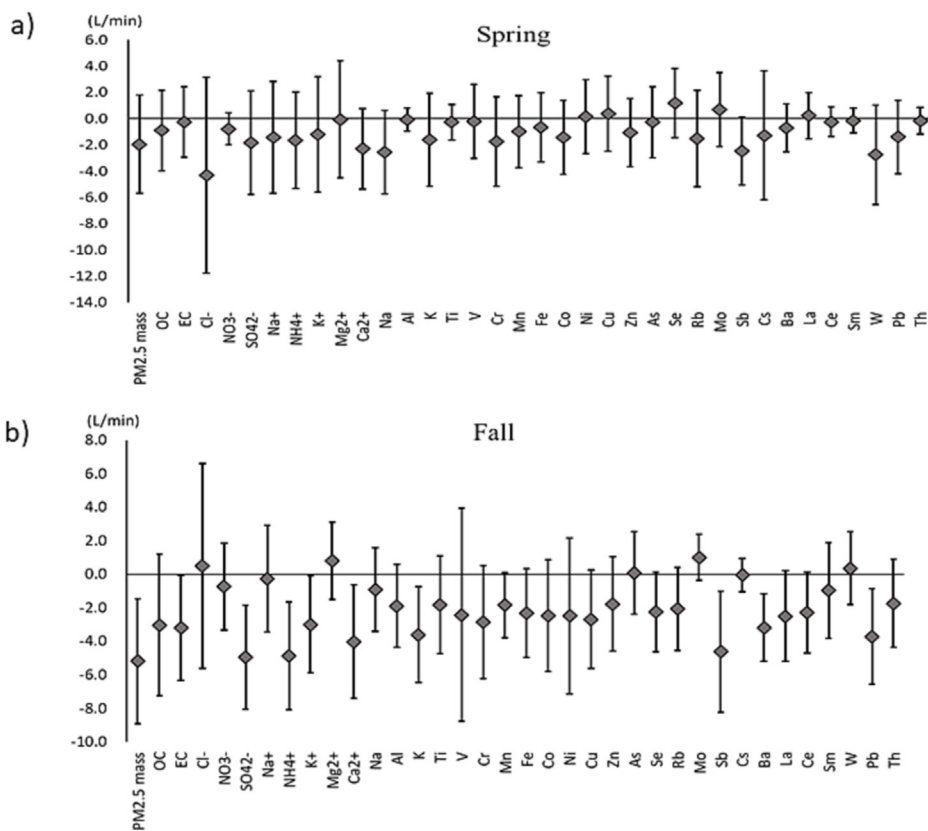


Fig. 2. Changes in peak expiratory flow (PEF) associated with increases in the interquartile range of each daily concentration of mass and chemical compositions of fine particulate matter ( $PM_{2.5}$ ).

The ionic components of  $PM_{2.5}$  have been associated with decreased pulmonary function in patients with COPD and healthy individuals (Zhou et al., 2021; Wu et al., 2013). Shi et al. (2016) found that the  $NO_3^-$ ,  $SO_4^{2-}$ ,  $NH_4^+$ , and  $K^+$  concentrations in  $PM_{2.5}$  were associated with increased FeNO, which is a marker of inflammatory response in the airway. In addition to the short-term studies, substantial associations have been observed between lower PEF and long-term exposure to  $NH_4^+$ ,  $SO_4^{2-}$ , and  $NO_3^-$  in  $PM_{2.5}$  (Yang et al., 2021). In the present study, the  $NO_3^-$ ,  $SO_4^{2-}$ ,  $NH_4^+$ , and  $K^+$  concentrations in  $PM_{2.5}$  were associated with decreased PEF and FEV<sub>1</sub> values, with  $SO_4^{2-}$  demonstrating the strongest association with decreased pulmonary function. A study conducted in Canada reported that an elevated  $SO_4^{2-}$  concentration in  $PM_{2.5}$  can significantly increase the risk of hospitalization owing to the development of respiratory disease (Burnett et al., 1995). Moreover, a significant association between  $SO_4^{2-}$  and the onset of new asthma has been documented (Abbey et al., 1993). In Japan, a large fraction of  $SO_4^{2-}$  in  $PM_{2.5}$  is derived from artificial sources, such as ship emissions; natural sources, such as seawater and volcanoes; and transboundary pollution from neighboring countries (Itahashi et al., 2017). This survey was conducted on an isolated island without major sources of artificial air pollution;  $SO_4^{2-}$  pollution in the surrounding area may be attributed to the presence of numerous ships in the Seto Inland Sea and transboundary air pollution from the Asian continent. Thus, high  $SO_4^{2-}$  concentrations affected the respiratory system even in healthy individuals.

Herein, our findings showed a significant association between pulmonary function and several elemental components of  $PM_{2.5}$ , with potassium showing the greatest effect. In a previous study conducted in California, the potassium concentration in  $PM_{2.5}$  was associated with the risk of hospitalizations due to development of a respiratory disease (Ostro et al., 2009). Zhang et al. (2020) have shown that the potassium concentration in  $PM_{2.5}$  was significantly associated with the release of interleukin-8 and monocyte chemoattractant protein-1 in healthy adults. Potassium, a biofuel, is a

metallic element that originates from fuel combustion occurring during the incineration of waste and plants. Considering the area where the present study was conducted, field burning was observed in the surrounding areas several times during the study period. Field burning was frequently performed in fall season, and crop residues and fallen leaves were burned. In an open-burning experiment in Japan, high potassium concentrations were emitted from extreme fire (Fushimi et al., 2017). Previous animal studies have shown that exposure to straw-burned  $PM_{2.5}$  worsened pulmonary inflammation and fibrosis and increased the risk of mortality in mice (Hu et al., 2017). The burning process caused the release of  $PM_{2.5}$  containing potassium into the atmosphere, which could have affected the respiratory system of students in nearby schools. Additionally, the concentrations of several transition metals, such as Cr and Mn, were significantly associated with reductions in the PEF and FEV<sub>1</sub> values. Transition metals are associated with oxidative stress-generating reactions (Ghio et al., 2012). Therefore, oxidative stress is generated by exposure to transition metals, leading to inflammation and damage, thereby affecting pulmonary function.

We have previously reported that the association between  $PM_{2.5}$  mass concentration and decreased respiratory function was more pronounced in fall than in spring (Yoda et al., 2019). Ito et al. (2011) suggested that the association between  $PM_{2.5}$  components and cardiovascular disease-related mortality and hospitalization varies by season; the composition of  $PM_{2.5}$  components also varies from season to season. Therefore, the source can distinctly impact the mortality and hospitalization risks. A previous study in China examined the  $PM_{2.5}$  composition and mortality risk, revealing that the EC and  $NO_3^-$  components of  $PM_{2.5}$  and mortality risk were strongly associated with the warm period, while  $SO_4^{2-}$  and  $NH_4^+$  were strongly associated with the cold period. These findings indicated a difference in the seasonal pattern among the  $PM_{2.5}$  components (Zhou et al., 2022). Our study examined the relationship between the  $PM_{2.5}$  components and the respiratory organs of healthy individuals. The mass concentrations

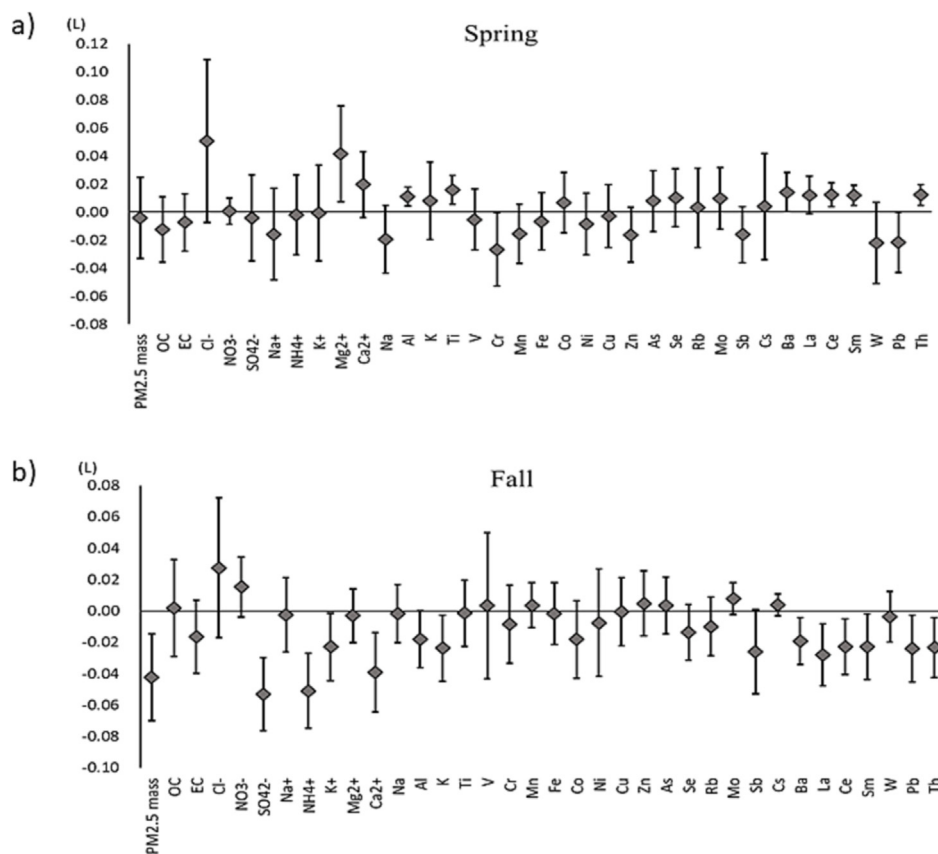


Fig. 3. Changes in forced expiratory volume in 1 s ( $FEV_1$ ) associated with increases in the interquartile range of each daily concentration of mass and the chemical compositions of fine particulate matter ( $PM_{2.5}$ ).

of  $PM_{2.5}$  were elevated during spring, although the effects of  $PM_{2.5}$  components on pulmonary function were more pronounced during fall. The differences in the effects of  $PM_{2.5}$  components by season are consistent with the results of Ito et al.'s (2011) study. The finding indicating the highly significant association of  $SO_4^{2-}$  concentration with pulmonary function is consistent with those of Chinese studies (Zhou et al., 2022). The association between PEF and Sb concentration was also observed during fall season. In Japan, Sb is reportedly generated from brake wear and ash from waste incineration (Iijima et al., 2009). The rate of brake wear is relatively low in the area where the survey was conducted owing to the low traffic volume. However, the presence of Sb may be attributed to the incineration of waste, considering that field burning was observed in surrounding areas. Exposure to high levels of Sb can cause coughing, shortness of breath, and pneumoconiosis (Potkonjak and Pavlovich, 1983). In previous animal studies, inflammation and fibrosis of the alveoli have been attributed to Sb accumulation in the lungs (Newton et al., 1994). As exposure to Sb may affect the lungs of healthy individuals, the regulation of field burning, which is the source of Sb, is necessary.

Certain components of  $PM_{2.5}$  that affect pulmonary function differ from those reported in previous studies. This discrepancy in the results may reflect the different effects of  $PM_{2.5}$  components on pulmonary function due to the variations in the sources by region and season. Despite the relatively low mass concentrations of  $PM_{2.5}$  in the present study area, a relationship was observed between mass concentration and certain components and decreased pulmonary function, indicating a short-term effect on the respiratory system. However, no association was detected between pulmonary function and concentration of Na, the third-highest elemental component in  $PM_{2.5}$ . Alternatively, pulmonary function was associated with exposure to relatively low constituent elements such as Cr, Mn, and Cu. Even in small concentrations (<0.1 %) of  $PM_{2.5}$  mass, these chemical components may adversely affect the respiratory organs of healthy individuals.

To prevent effects on the respiratory system, the sources of these components should be identified, and efforts should be made to reduce their concentration.

Our study has several strengths. Repeated surveys of the same participants over a 3-year period using an electronic peak flow meter led to the performance of >4000 tests, thus enabling the analysis of effects mediated by small changes in the component concentrations in areas with relatively low  $PM_{2.5}$  concentrations. In addition, the accurate exposure assessment could be performed by collecting a sample of  $PM_{2.5}$  on the rooftop of a school where the students under evaluation spend a considerable period. Nevertheless, this study has some limitations. First, the data of four elements could not be used as the concentrations analyzed were below the lower limit of detection. However, it was possible to perform detailed analyses of the relationships between  $PM_{2.5}$  chemical components and pulmonary function by obtaining the results of 8 ion components and 25 elemental components. Second, the present study was conducted on an isolated island in the Seto Inland Sea. The compositions of  $PM_{2.5}$  components depend largely on the source and vary depending on the region, location, and timing; hence, the present results are non-generalizable. Third, as this survey targeted students, it was only conducted during spring and fall owing to the long holidays. As the composition of  $PM_{2.5}$  varies according to the season, the survey should be conducted throughout the year.

## 5. Conclusion

This repeated panel study conducted within two and a half years indicated that several chemical components of  $PM_{2.5}$  were associated with decreased pulmonary function in healthy adolescents in an isolated island without major artificial sources of air pollution. Even in the area with relatively low  $PM_{2.5}$  concentrations, the effects of  $PM_{2.5}$  chemical components on the pulmonary function of exposed healthy adolescents varied

depending on the type of substance. Especially,  $\text{SO}_4^{2-}$  among the ionic components and K concentration among the elemental components had the greatest impact. In addition, the concentration of  $\text{PM}_{2.5}$  components differed depending on the season, and the effects of many chemical components of  $\text{PM}_{2.5}$  on pulmonary function were more prominent in fall than in spring. Among the metallic elements, the effect of Sb was greatest during fall season. Some chemical components of  $\text{PM}_{2.5}$  adversely affect the pulmonary function of healthy adolescents, and the specific components have a large role in the effects of  $\text{PM}_{2.5}$ . If the sources of such components could be identified, their potential adverse health effects may be prevented by public health measures to reduce the levels of identified substances.

### CRedit authorship contribution statement

**Satoru Kobayashi:** Formal analysis, Writing – original draft, Writing – review & editing. **Yoshiko Yoda:** Validation, Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Hiroshi Takagi:** Software, Investigation. **Takeshi Ito:** Investigation. **Junko Wakamatsu:** Investigation, Data curation. **Ryohei Nakatsubo:** Investigation, Data curation. **Yosuke Horie:** Investigation. **Takatoshi Hiraki:** Investigation, Methodology, Resources. **Masayuki Shima:** Conceptualization, Methodology, Supervision, Project administration, Funding acquisition.

### Data availability

Data will be made available on request.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2023.165195>.

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