Environ Sci Pollut Res
DOI 10.1007/s11356-016-7228-6

RESEARCH ARTICLE

Haze is a risk factor contributing to the rapid spread of respiratory syncytial virus in children

Qing Ye[1] · Jun-fen Fu[1] · Jian-hua Mao[1] · Shi-qiang Shang[1,2]

Received: 3 March 2016 / Accepted: 11 July 2016

Abstract This study investigated whether respiratory syncytial virus (RSV) infection in children was associated with ambient temperature and air pollutants in Hangzhou, China. A distributed lag non-linear model (DLNM) was used to estimate the effects of daily meteorological data and air pollutants on the incidence of RSV infection among children. A total of 3650 childhood RSV infection cases were included in the study. The highest air pollutant concentrations were in January to May and October to December during the year. The yearly RSV-positive rate was 10.0 % among children with an average age of 4.3 months. The highest RSV-positive rate occurred among patients 0 to 3 months old. Children under 6.5 months old accounted for 80 % of the total patients infected by RSV. A negative correlation was found between ambient temperature and RSV infection, and it was strongest with minimum ambient temperature ($r = -0.804$, $P < 0.001$). There was a positive correlation between the infection rate and the particulate matter (PM) 2.5 ($r = 0.446$, $P < 0.001$), PM10 ($r = 0.397$, $P < 0.001$), SO_2 ($r = 0.389$, $P < 0.001$), NO_2 ($r = 0.365$, $P < 0.001$) and CO ($r = 0.532$, $P < 0.001$). The current study suggested that temperature was an important factor associated with RSV infection among children in Hangzhou. Air pollutants significantly increased the risk of RSV infection with dosage, lag and cumulative effects.

Keywords Air pollution · Particulate matter · Respiratory syncytial virus

Communicated by: Philippe Garrigues

✉ Shi-qiang Shang
yeqingkaoyan@163.com

1 Zhejiang Key Laboratory for Neonatal Diseases, The Children's Hospital of Zhejiang University School of Medicine, Hangzhou, People's Republic of China

2 Clinical Laboratory, The Children's Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China

Introduction

Although the government has created some environmental policies that limit the levels of certain air pollutants, there are still a number of adverse health effects that are caused by exposure to these agents. Numerous epidemiological studies have noted an association between air pollution levels and hospital admissions for a variety of different health problems (including a number of respiratory diseases) and an increased morbidity and mortality associated with various cardiovascular diseases (Langrish et al. 2014; Lin et al. 2013; Tong et al. 2014; Wong et al. 2014). Because respiratory virus infections largely impact morbidity and even mortality, it is important to understand whether and how exposure to common air pollutants exacerbates the susceptibility to and the severity of respiratory virus infections. Respiratory syncytial virus is a respiratory virus that can cause severe infection among infants and young children, and it is the leading cause of bronchiolitis in children under 1-year-old around the world (Halasa et al. 2015; Ye et al. 2015). RSV outbreaks also cause a significant increase in hospital admissions during the winter (Piedimonte and Perez 2014). To clarify the relationship between air quality and RSV infection, this study applied a distributed lag non-linear model to assess the effects of the daily meteorological data and air pollutants on the risk of RSV infection among children.

Published online: 20 July 2016

Objects and methods

Study subjects

To study the correlation between air quality and RSV infection, a prospective study was performed from January 1, 2015 to December 31, 2015. During this period, 100 nasopharyngeal secretion specimens were collected each day from patients with respiratory tract infections at the paediatric outpatient department in Hangzhou. The RSV-positive samples were detected by direct immunofluorescence assays and then used to calculate the RSV-positive rate per day. Additionally, meteorological data and atmospheric pollutant data from Hangzhou were collected from the online air quality detection analysis platform (http://www.aqistudy.cn/). The meteorological data included the daily maximum temperature, minimum temperature, average temperature, temperature variance and relative humidity. The atmospheric pollutant data included the daily AQI index and PM2.5, PM10 , CO, NO_2 and SO_2 concentrations. A statistical method was employed to assess the effects of daily meteorological data and air pollutants on the risk of RSV infection among children. The study was approved by the medical ethics committee of the Children's Hospital of Zhejiang University School of Medicine. Written informed consent was obtained from the guardians of the child participants who were enrolled in the study.

Method for RSV detection

The respiratory syncytial virus from nasopharyngeal swabs was detected using the D3 Ultra DFA Respiratory Virus Screening and ID kit (Diagnostic Hybrids, Athens, USA). On each well of a two-well and an eight-well slide, 25 μL of the prepared cell suspension, collected from nasopharyngeal swabs was spotted. This step was repeated for each specimen. The wells were allowed to air dry completely. The cells were fixed onto the slides using fresh, chilled 100 % acetone for 5 to 10 min at 20° to 25 °C. Afterwards, the fixative was removed, and the slides were air dried. One drop of the DFA screening reagent was added to completely cover the dried, fixed cells in each of the two-well slides and in each well of a fresh respiratory virus antigen control slide. The antigen control slide was stained only once, as it contained individual wells of viral infected cells and non-infected cells. One drop of normal mouse gamma globulin DFA reagent was also added to completely cover the dried, fixed cells on one well of each two-well slide. The slides were then placed in a covered, humidified chamber at 35 °C to

Table 1 RSV infection rate, atmospheric environment and meteorological conditions in Hangzhou, 2015

Variables	Criterion value	Mean	Standard deviation	Minimum	Percentile			Maximum	*r*	*P*
					25th	50th	75th			
Air pollutions										
AQI	50[b]	79.5	36.6	20.0	55.0	71.0	97.0	272.0	0.403	<0.001
PM2.5 (μg/m^3)	10[b]	53.9	30.6	8.0	32.0	48.0	68.0	224.0	0.446	<0.001
PM10 (μg/m^3)	20[b]	80.6	41.0	11.0	51.5	72.0	100.0	283.0	0.397	<0.001
SO2 (μg/m^3)	20[a]	14.5	6.9	4.0	9.0	13.0	18.0	43.0	0.389	<0.001
NO2 (μg/m^3)	40[b]	44.4	16.2	11.0	33.0	42.0	53.0	96.0	0.365	<0.001
CO (μg/m^3)	10[c]	0.9	0.3	0.4	0.7	0.8	1.0	2.0	0.532	<0.001
Weather										
Minimum temperature (°C)		14.1	8.1	−2.0	6.5	15.0	21.0	28.0	−0.804	<0.001
Maximum temperature (°C)		22.1	8.4	3.0	15.0	24.0	29.0	39.0	−0.699	<0.001
Mean temperature (°C)		18.1	8.0	2.0	11.3	19.5	24.5	33.5	−0.772	<0.001
Temperature variations (°C)		8.0	3.9	1.0	6.0	8.0	10.0	27.0	0.175	0.001
Relative humidity (%)		73.8	14.5	28.0	64.0	75.0	87.0	97.0	−0.137	0.009
Amount of precipitation (mm)		4.0	9.0	0.0	0.0	0.0	4.0	86.0	−0.138	0.008
Disease										
RSV-positive rate (%)		10.4	12.0	0.0	0.0	5.1	18.2	52.0		

Temperature variance refers to the daily temperature difference

[a] Twenty-four-hour mean from "WHO air quality guidelines"

[b] Annual mean from "WHO air quality guidelines"

[c] Maximum daily 8-hour mean from "on ambient air quality and cleaner air for Europe"

37 °C for 15 to 30 min. Then, the stained cells were rinsed using a ×1 wash solution and de-mineralized water. The stained, mounted cells were examined with a fluorescence microscope at magnifications from ×200 to ×400. If the slide was positive for the respiratory virus, the staining procedure was repeated using the reserved eight-well specimen slide to identify whether respiratory syncytial virus was present.

Statistical analysis

The distributed lag non-linear model is a time sequence model based on generalized linear models and generalized additive models, which are advantageous for analysing the lag effect and cumulative effect in non-linear processes. Consequently, this model was adopted to fit the experimental data. Please refer to reference (Gasparrini and Leone 2014) for details. The daily RSV-positive rate was used as the dependent variable, and a cross matrix was created with the daily pollutant concentrations, temperature and lag time. The confounding effects of holiday effects, relative humidity, day of the week and long-term trends were controlled to analyse the relationship between the daily pollutant concentrations, the temperature and the RSV-positive rate. The model formula was as follows: $\mathrm{LogE}\,[Yt] = a1\mathrm{crossbasis}1 + \mathrm{ns}(x1, df) + a2\mathrm{crossbasis}2 + a3\mathrm{crossbasis}3 + a4\mathrm{crossbasis}4 + a5\mathrm{crossbasis}5 + a6\mathrm{crossbasis}6 + \beta 1x2 + \gamma 1x3 + \gamma 2x4 + \delta$, where Yt is the RSV-positive detection rate on the observation date t, and crossbasis1 is the cross matrix created with the daily pollutant concentrations, temperature and maximum lag days in the DLNM software package. The daily temperature and PM2.5, PM10, SO_2, NO_2 and CO concentrations were evaluated in the model. The variable "ns" is the natural cubic spline function, df is the degree of freedom confirmed by the Akaike information criterion (AIC), and x1 is the time sequence variable that controls the long-term trend. Crossbasis 2–6 are five additional variables excluding the variable substituted for dividing crossbasis1. The variable x2 describes the relative humidity of the same period, and β1 is its coefficient. The dummy variable x3 describes the day of week, and γ1 is its coefficient. The variable x4 describes whether t is a holiday, defined by the Chinese government website and including legal holidays, such as the Spring Festival, National Day and Tomb-Sweeping Day; γ2 is its coefficient. The term "δ" is a constant of the model. Data manipulation and all statistical analyses were performed using SPSS18.0 statistical software and statistical environment R 3.2.3 (DLNM 2.1.3 package). Relative risk (RR) is the ratio of the probability of RSV infection occurring in an exposed group to the probability of the event occurring in a comparison, non-exposed group.

Results

Characteristics of RSV-infected patients and the atmospheric environment and meteorological conditions in Hangzhou in 2015

The average temperature of Hangzhou in 2015 was 18.1 °C, the minimum temperature was −2 °C, and the maximum temperature was 39 °C. The average relative humidity throughout

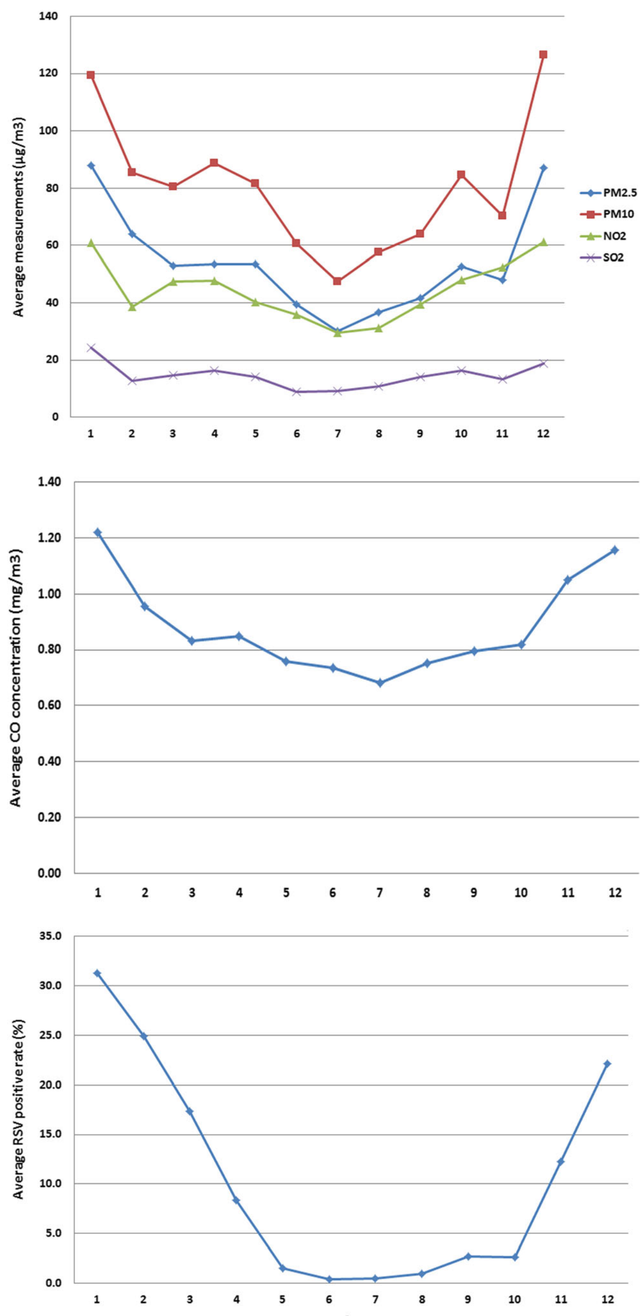

Fig. 1 Patterns of the respiratory syncytial virus (RSV)-positive rate among children and the concentrations of air pollutants by month in Hangzhou, 2015

the year was 73.8 %. The major air pollutants were PM2.5 and PM10, which were five times and four times higher, respectively, than the WHO standard (Table 1). The highest air pollutant concentrations were recorded from January to May and from October to December (Fig. 1). This study included 36,500 cases of children with respiratory tract infection, and there were 3650 RSV positive patients; thus, the positive rate was 10.0 %. Among the RSV-positive patients, there were 2343 males and 1307 females and the ratio of males to females was 1.8:1. The average age was 4.3 months, and the standard deviation of the age distribution was 7.9 months. Patients 0 to 3 months old had the highest RSV-positive rate. Children under 6.5 months old accounted for 80 % of the total patients infected by RSV, and approximately 95 % of RSV-positive children were younger than 10.5 months old (Fig. 2). The high-incidence seasons of RSV infection were from January to March and December (Fig. 3).

The relationship between ambient temperature and RSV infection

There was a negative correlation between ambient temperature and the RSV infection rate. The strongest correlation was between minimum ambient temperature and RSV infection rate ($r = -0.804$, $P < 0.001$) (Table 1). When the minimum ambient temperature was below 9 °C, the RSV-positive detection rate was greater than 20 %; however, when the minimum temperature was higher than 20 °C, the positive rate was lower than 5 % (Fig. 3). There was an evident lag effect of the ambient temperature impact on the RSV detection rate. Generally, the maximum impact of ambient temperature variation on the detection of RSV occurred at lag 4 day, and the maximum RR was approximately 1.4. Using 20 °C as the reference, the cumulative effect decreased gradually with an increase in ambient temperature. In 2015, the cumulative relative risk caused by the maximum cumulative effect due to the ambient temperature drop was 1.8 at 6 °C.

The relationship between air pollutants and RSV infection

There was a positive correlation between the RSV infection rate and PM2.5 ($r = 0.446$, $P < 0.001$), PM10 ($r = 0.397$, $P < 0.001$), SO_2 ($r = 0.389$, $P < 0.001$), NO_2 ($r = 0.365$, $P < 0.001$) and CO ($r = 0.532$, $P < 0.001$). When the concentration of PM2.5 was over 150 μg/m^3, it started to affect RSV infection rates, and the relative risk gradually decreased with the increase of lag days. Elevated PM10 concentrations were not immediately harmful but were after a lag of 3 days. Both PM2.5 and PM10 concentrations had no significant cumulative effect on RSV infection rates. NO_2 and SO_2 pollution levels showed the greatest relative risk of RSV infection at a lag of approximately 3 days. With increased SO_2 concentration, relative risk gradually increased, and when NO_2 concentrations exceeded 40 μg/m^3, relative risk of RSV infection was attenuated; however, both pollutants had no significant cumulative effect. CO showed a higher risk at low concentrations and its RR increased with increased CO concentrations. There was a lag effect such that the relative risk gradually decreased with an increase of lag days. The strongest cumulative effect occurred when the CO concentration was 1.5 mg/m^3; the RR was approximately 2. (Figs. 4 and 5).

Discussion

This study included 36,500 children with respiratory tract infections, and the respiratory syncytial virus-positive detection rate was 10 %. In the USA, the RSV infection rates of patients that led to emergency department and paediatric practice visits were 28 in 1000 and 8 in 1000, respectively (Hall et al. 2009); both showed a high RSV infection rate. Additionally, our research showed that males were more susceptible because the ratio of RSV-infected males to females was 1.8:1. The average age of infected children was 4.3 months, and the standard deviation of the age distribution was 7.9 months. Children

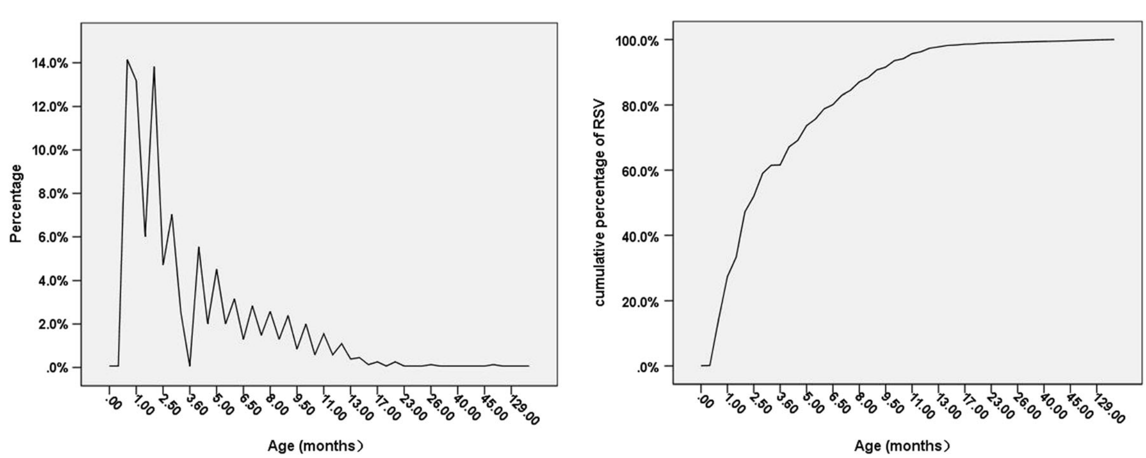

Fig. 2 Age distribution of RSV infected children

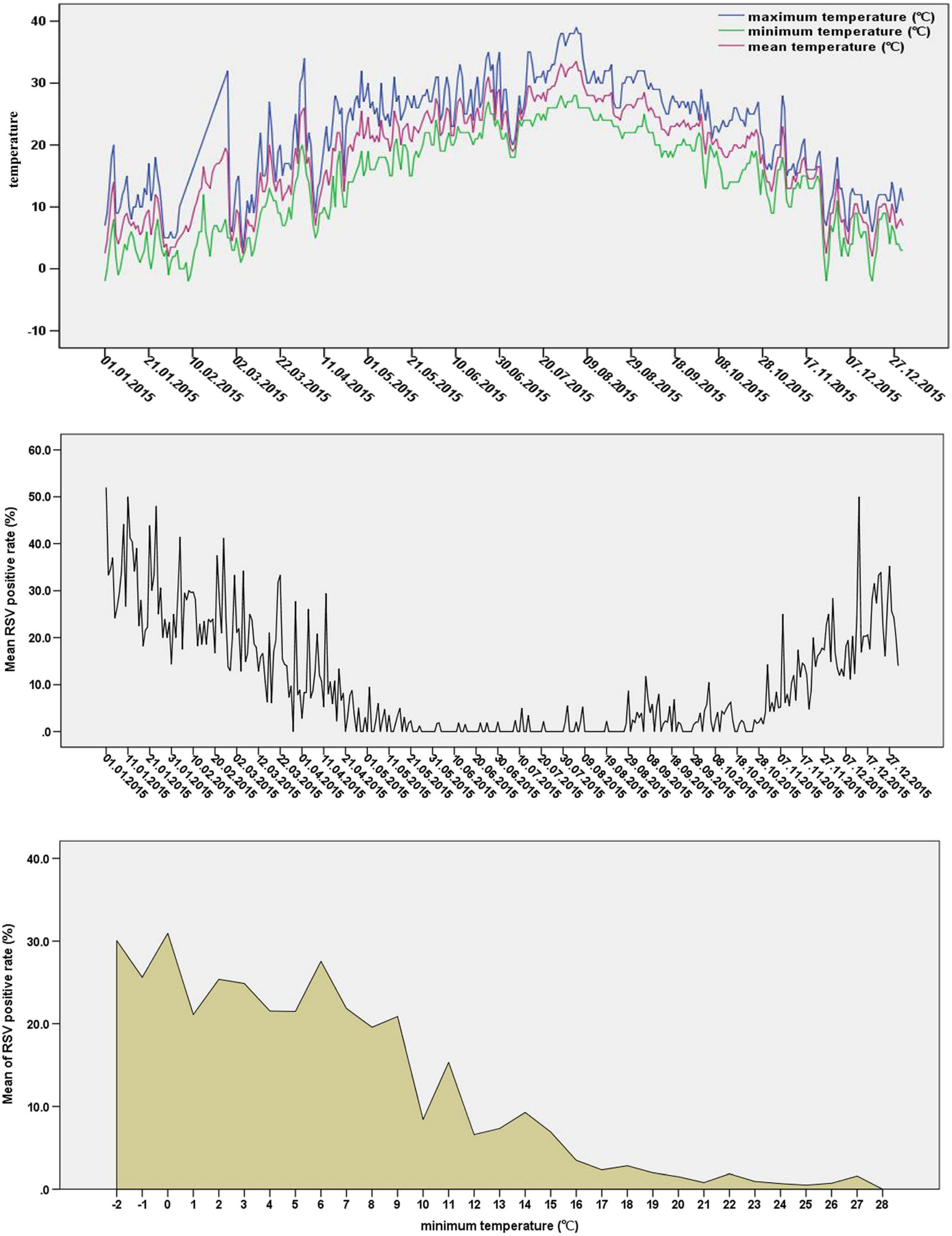

Fig. 3 Patterns of the RSV positive rate among children and the ambient temperature in Hangzhou, 2015

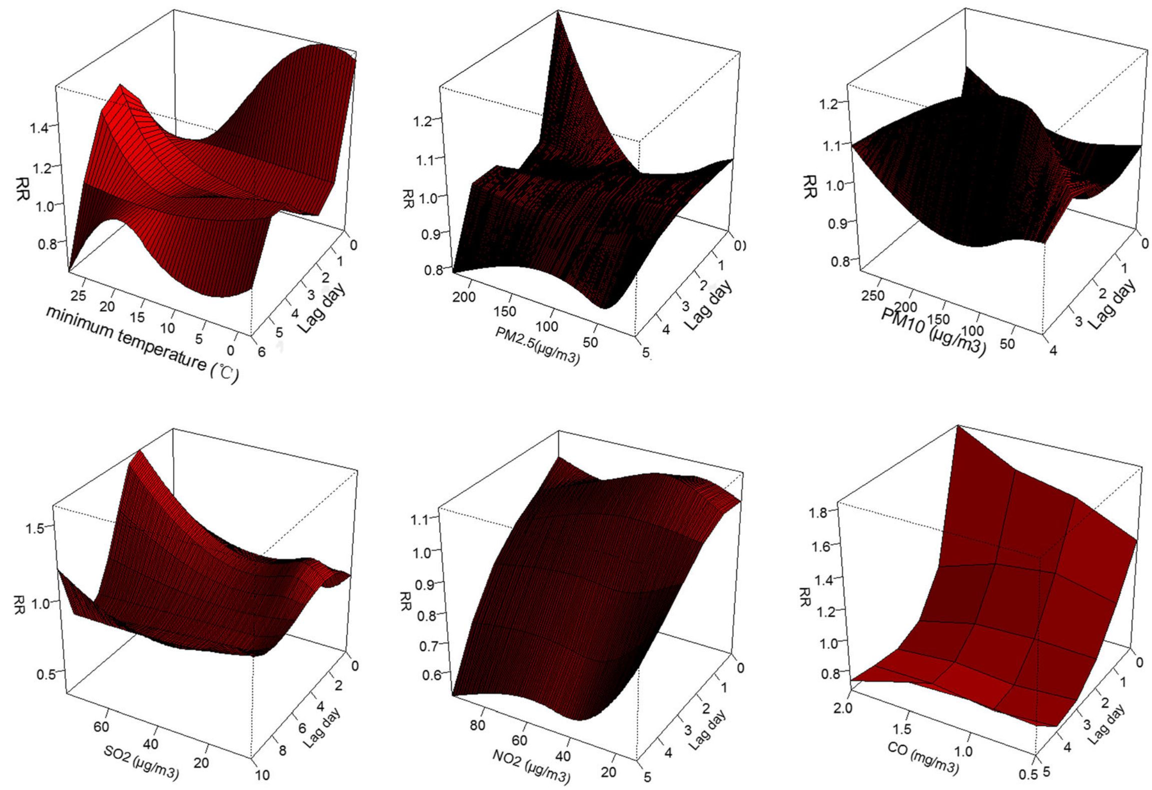

Fig. 4 Lag associations and dose effect between ambient temperature (baseline: 20 °C)/air pollutants and RSV infection rate. The distributed lag non-linear model (DLNM) model controlled for the effects of holiday effects, relative humidity, day of the week and long-term trends

younger than 6.5 months accounted for 80 % of the total RSV-infected patients, and approximately 95 % of the RSV-positive children were younger than 10.5 months old, which was similar to that reported by other studies (Panayiotou et al. 2014; Rodriguez-Martinez et al. 2015). In addition, children aged 0 to 3 months had the highest RSV-positive rate, which may be related to their immature immune system. Our results also suggested that infants cannot obtain the effective antibodies maternally to avoid RSV infection.

According to our study, the highest months of RSV infection incidence in Hangzhou were from January to March and December; these months were also the coldest periods of the year in this area. There was a negative correlation between ambient temperature and RSV infection rate. The strongest correlation was found between the minimum temperature and the RSV infection rate ($r = -0.804$, $P < 0.001$). When the minimum ambient temperature was below 9 °C, the RSV-positive detection rate was greater than 20 %; when the

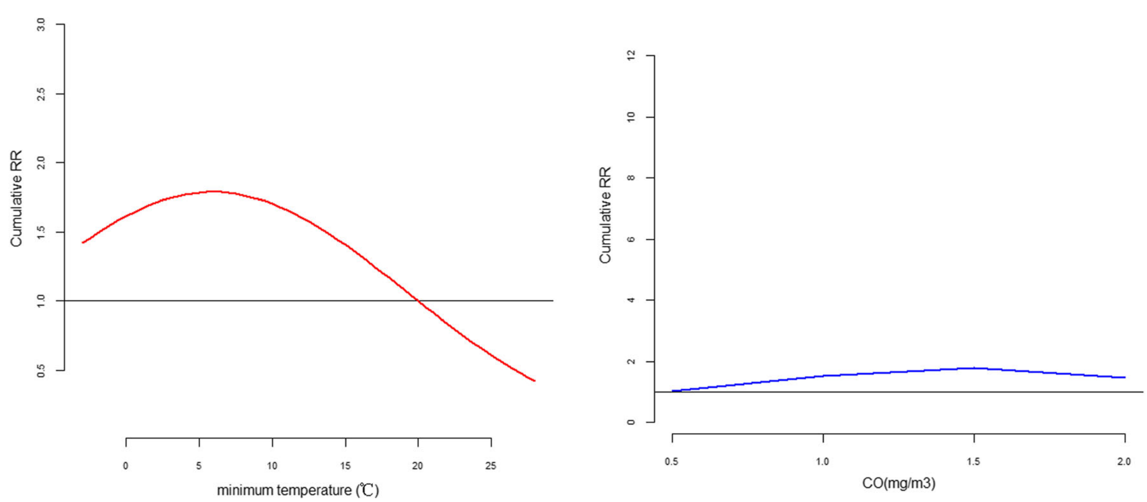

Fig. 5 Cumulative relative risks for minimum temperature and CO associated with the RSV infection rate using the DLNM model, which controlled for the effects of holiday effects, relative humidity, day of the week and long-term trends

minimum ambient temperature was higher than 20 °C, the RSV-positive detection rate was less than 5 %. Therefore, ambient temperature was an important factor that impacted the prevalence of RSV in Hangzhou, similar to that of studies in other geographical areas (Paynter et al. 2014; Pica and Bouvier 2014; Vandini et al. 2013). Additionally, there was a lag effect between ambient temperature and RSV detection rate. Generally, the maximum impact of ambient temperature variation on RSV detection occurred on lag 4 day, and the maximum RR was approximately 1.4. With 20 °C as the reference, the cumulative effect decreased gradually with an increase in ambient temperature. In 2015, the cumulative relative risk caused by the maximum cumulative effect of temperature drops was 1.8 at 6 °C. However, the mechanism by which the temperature drop increased the risk of RSV infection among children remains unclear. Based on laboratory evidence (Moe and Harper 1983), low temperature may prolong virus survival in the environment, which increases the possibility of infectious virus exposure.

In 2015, the regional gross domestic product (GDP) of Hangzhou was 1005.358 billion Yuan, making Hangzhou the tenth city exceeding 1000 billion Yuan in GDP across China. In comparison, the year-to-year growth was 10.2 %. This high-speed economic development also caused abundant environmental problems, including severe haze. Air pollutants, such as PM2.5, PM10, SO_2, NO_2 and CO, were usually above the limits. The primary air pollutants in Hangzhou were PM2.5 and PM10, and their average levels exceeded the WHO standard by five times and four times, respectively, in 2015. From January to May and from October to December, the airflow was relatively stable in Hangzhou, and it was attenuated the spread of pollutants. As a result, these months had the highest concentrations of air pollutants. This period coincided with the high-incidence months (January to March and December) of RSV infection in Hangzhou. In addition, the finding that air pollution impacted the morbidity of RSV among children is advantageous for clinical practice. Generally, after the deterioration of air quality, the number of patients with bronchiolitis due to RSV increases significantly. If air pollution occurred for an extended period of time, it may cause a small peak in the occurrence of RSV. This study applied a distributed lag non-linear model to assess the effects of air pollutants on the RSV-positive rate among outpatient children.

The results of this study showed that there was a positive correlation between the concentrations of air pollutants, such as CO, SO_2, PM2.5, PM10 and NO_2, and the morbidity of RSV. These pollutants significantly increased the relative risk of RSV infection among children. Moreover, this impact was characterized by an evident dosage, lag and cumulative effect. Many studies showed that air pollution could cause a high incidence of respiratory disease (Gordon et al. 2014; Liang et al. 2014; Walton et al. 2010; Xu et al. 2013), but what the potential mechanisms mediating these effects are remain unknown (Ciencewicki and Jaspers 2007). It is believed that oxidative stress induced within an individual can have a wide range of effects on immunity as well as a variety of other processes. All of the pollutants evaluated herein have been shown to induce oxidative stress, and exposure to these agents may result in the production of free radicals, which can have damaging effects on the lungs (Hochscheid et al. 2005; Jaspers et al. 2005). Air pollutants may modulate a host's antiviral defences. Studies have shown that exposure to air pollutants can reduce the ability of macrophages to phagocytize (Hiraiwa and van Eeden 2013; Rylance et al. 2015). Additionally, surfactant proteins play an important part of the innate immune defence against respiratory viruses; studies conducted by our lab, as well as by others, have shown that exposure to air pollutants can decrease the expression and alter the function of hydrophilic surfactant proteins, such as SP-A and D (Silveyra and Floros 2012), which are associated with enhanced susceptibility to respiratory virus infections. Moreover, these effects are increased in the paediatric population, especially among young infants, because they have a higher respiratory rate and, therefore, inhale more pollutants per kilogram of body weight. In conclusion, air pollutants significantly increased the risk of RSV infection, and dosage, lag and cumulative effects were observed. However, the risk of RSV infection caused by air pollution still needs to be verified by additional clinical studies and experimental data.

Compliance with ethical standards The study was approved by the medical ethics committee of the Children's Hospital of Zhejiang University School of Medicine. Written informed consent was obtained from the guardians of the child participants who were enrolled in the study.

Funding This project was supported by grants from the National Natural Science Foundation of China (Grant No. 81501760), Zhejiang Provincial Natural Science Foundation of China (Grant No. LQ16H050002) and Zhejiang Provincial Healthy Science Foundation of China (Grant No. 2015KYB191). The funders did not take part in the study.

Author contributions Conceived and designed the experiments: Shi-qiang Shang. Performed the experiments: Jun-fen Fu, Jian-hua Mao and Shi-qiang Shang. Analysed the data: Jun-fen Fu. Contributed reagents/materials/analysis tools: Jun-fen Fu, Jian-hua Mao and Shi-qiang Shang. Wrote the paper: Qing Ye.

Conflicts of interest The authors declare that they have no conflict of interest.

References

Ciencewicki J, Jaspers I (2007) Air pollution and respiratory viral infection. Inhal Toxicol 19:1135–1146

Gasparrini A, Leone M (2014) Attributable risk from distributed lag models. BMC Med Res Methodol 14:55

Gordon SB et al. (2014) Respiratory risks from household air pollution in low and middle income countries. Lancet Respir Med 2:823–860

Halasa N, Williams J, Faouri S, Shehabi A, Vermund SH, Wang L, Fonnesbeck C, Khuri-Bulos N (2015) Natural history and epidemiology of respiratory syncytial virus infection in the Middle East: hospital surveillance for children under age two in Jordan. Vaccine 33:6479–6487

Hall CB, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, Auinger P, Griffin MR, Poehling KA, Erdman D, Grijalva CG, Zhu Y, Szilagyi P (2009) The burden of respiratory syncytial virus infection in young children. N Engl J Med 360:588–598

Hiraiwa K, van Eeden SF (2013) Contribution of lung macrophages to the inflammatory responses induced by exposure to air pollutants. Mediat Inflamm 2013:619523

Hochscheid R, Schuchmann U, Kotte E, Kranz S, Heinrichs S, Muller B (2005) NO2-induced acute and chronic lung injury cause imbalance of glutathione metabolism in type II pneumocytes. Med Sci Monit: Int Med J Exp Clin Res 11:Br273–Br279

Jaspers I, Ciencewicki JM, Zhang W, Brighton LE, Carson JL, Beck MA, Madden MC (2005) Diesel exhaust enhances influenza virus infections in respiratory epithelial cells. Toxicol Sci: Off J Soc Toxicol 85:990–1002

Langrish JP, Watts SJ, Hunter AJ, Shah AS, Bosson JA, Unosson J, Barath S, Lundback M, Cassee FR, Donaldson K, Sandstrom T, Blomberg A, Newby DE, Mills NL (2014) Controlled exposures to air pollutants and risk of cardiac arrhythmia. Environ Health Perspect 122:747–753

Liang Y, Fang L, Pan H, Zhang K, Kan H, Brook JR, Sun Q (2014) PM2.5 in Beijing - temporal pattern and its association with influenza. Environ Health : Glob Access Sci Source 13:102

Lin YK, Chang CK, Chang SC, Chen PS, Lin C, Wang YC (2013) Temperature, nitrogen dioxide, circulating respiratory viruses and acute upper respiratory infections among children in Taipei, Taiwan: a population-based study. Environ Res 120:109–118

Moe K, Harper GJ (1983) The effect of relative humidity and temperature on the survival of bovine rotavirus in aerosol. Arch Virol 76:211–216

Panayiotou C, Richter J, Koliou M, Kalogirou N, Georgiou E, Christodoulou C (2014) Epidemiology of respiratory syncytial virus in children in Cyprus during three consecutive winter seasons (2010–2013): age distribution, seasonality and association between prevalent genotypes and disease severity. Epidemiol Infect 142: 2406–2411

Paynter S, Sly PD, Ware RS, Williams G, Weinstein P (2014) The importance of the local environment in the transmission of respiratory syncytial virus. Sci Total Environ 493:521–525

Pica N, Bouvier NM (2014) Ambient temperature and respiratory virus infection. Pediatr Infect Dis J 33:311–313

Piedimonte G, Perez MK (2014) Respiratory syncytial virus infection and bronchiolitis. Pediatr Rev / Am Acad Pediatr 35:519–530

Rodriguez-Martinez CE, Rodriguez DA, Nino G (2015) Respiratory syncytial virus, adenoviruses, and mixed acute lower respiratory infections in children in a developing country. J Med Virol 87:774–781

Rylance J, Fullerton DG, Scriven J, Aljurayyan AN, Mzinza D, Barrett S, Wright AK, Wootton DG, Glennie SJ, Baple K, Knott A, Mortimer K, Russell DG, Heyderman RS, Gordon SB (2015) Household air pollution causes dose-dependent inflammation and altered phagocytosis in human macrophages. Am J Respir Cell Mol Biol 52:584–593

Silveyra P, Floros J (2012) Air pollution and epigenetics: effects on SP-A and innate host defence in the lung. Swiss Med Wkly 142:w13579

Tong L, Li K, Zhou Q (2014) Promoted relationship of cardiovascular morbidity with air pollutants in a typical Chinese urban area. PLoS One 9:e108076

Vandini S, Corvaglia L, Alessandroni R, Aquilano G, Marsico C, Spinelli M, Lanari M, Faldella G (2013) Respiratory syncytial virus infection in infants and correlation with meteorological factors and air pollutants. Ital J Pediatr 39:1–6

Walton NA, Poynton MR, Gesteland PH, Maloney C, Staes C, Facelli JC (2010) Predicting the start week of respiratory syncytial virus outbreaks using real time weather variables. BMC Med Inform Decis Mak 10:1–9

Wong MC, Tam WW, Wang HH, Lao XQ, Zhang DD, Chan SW, Kwan MW, Fan CK, Cheung CS, Tong EL, Cheung NT, Tse LA, Yu IT (2014) Exposure to air pollutants and mortality in hypertensive patients according to demography: a 10 year case-crossover study. Environ Pollut (Barking, Essex : 1987) 192:179–185

Xu Z, Hu W, Williams G, Clements AC, Kan H, Tong S (2013) Air pollution, temperature and pediatric influenza in Brisbane, Australia. Environ Int 59:384–388

Ye Q, Shao WX, Shang SQ, Pan YX, Shen HQ, Chen XJ (2015) Epidemiological characteristics and immune status of children with respiratory syncytial virus. J Med Virol 87:323–329