Original article

Epidemiological characteristics and meteorological factors of childhood *Mycoplasma pneumoniae* pneumonia in Hangzhou

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Background: ***Mycoplasma pneumoniae* (*M. pneumoniae*) is an important pathogen of pediatric respiratory infections and the relation of *M. pneumoniae* pneumonia (MPP) with meteorological factors remains obscure. This study aims to investigate the epidemiological characteristics of childhood MPP and observe if there is a relationship between epidemiological characteristics and meteorological factors in Hangzhou.**

Methods: ***M. pneumoniae* DNA in nasopharyngeal aspirates of hospitalized pneumonia children were detected by polymerase chain reaction from January 1, 2007 to December 31, 2009. The positive rates of MPP (MPP rates) in different years, seasons and ages were compared. The relationship between MPP rates and meteorological data, including mean air temperature (ºC), mean relative humidity (%), monthly precipitation (mm) and raining days were analyzed.**

Results: **In 14 799 pneumonia cases found from 2007 to 2009, the MPP rate was 18.5%. Altogether 1610 boys (16.9%) and 1134 girls (21.4%) suffered from MPP with a significant difference between both genders (χ^2=45.68, P<0.001). In children younger than 1 year, 1-2 years, 3-6 years, and older than 7 years, the MPP rates were 9.8%, 21.1%, 44.4% and 61.6%, respectively. The MPP rates were significantly higher in older children than in younger ones (trends test χ^2=46.72, P<0.001). In a descending order, the MPP rates in summer, autumn, spring, and winter were 27.8%, 23.9%, 18.0% and 11.6%, respectively (χ^2=372.75, P<0.001). The MPP rates in 2007 to 2009 were 12.9%, 19.3% and 23.6%, respectively (trends test χ^2=13.72, P<0.001). Of the four meteorological factors, only monthly mean air temperature was included in the multiple linear regression model (P<0.001).**

Conclusions: **This study showed that the MPP rate was higher in older children than in younger ones. Girls had a higher positive rate of MPP than boys. In Hangzhou, MPP was more prevalent in summer and autumn. Air temperature was the only meteorological factor affecting the prevalence of MPP.**

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Key words: **meteorological factor; *Mycoplasma pneumoniae*; pneumonia; temperature**

Introduction

Mycoplasma pneumoniae (*M. pneumoniae*) is a kind of prokaryotic microbe with a size between virus and bacteria. It is a common pathogen of primary atypical pneumonia and other respiratory infectious diseases. Except respiratory tract infections, *M. pneumoniae* also causes multiple system complications and immune dysfunction or immune damage.[1,2] In recent years the incidence of *M. pneumoniae* pneumonia (MPP) has risen, and reports on macrolide-resistant *M. pneumoniae* have been increasing.[3,4] Refractory or critical MPP cases are also seen increasingly, with a great harm to children, especially those with weak immune function. Different weather conditions affect microorganisms, including *M. pneumoniae*. There are studies on the relationship of meteorological factors and *M. pneumoniae* infections, but none has been conducted in Hangzhou. Different studies have different conclusions on the seasonal or

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climate effects.[5-8] The present study aims to investigate the epidemiological characteristics of MPP in Hangzhou and to observe the relationship between meteorological factors and MPP.

Methods

Patients

This retrospective study was conducted in the Children's Hospital, Zhejiang University School of Medicine, Hangzhou, China, from January 2007 to December 2009. Hangzhou, which has a population of 7 million, is situated in southeast China at 120.2E, 30.3N. Located in subtropical monsoon climate district, it has four distinctive seasons: spring (March to May), summer (June to August), autumn (September to November), and winter (December to the next February). The average annual temperature varies from 15.9ºC to 17.0ºC, with a maximum of 28.4ºC in July and a minimum of 4.3ºC in January. The relative humidity is 71.0%±6.0%.

A total of 14 799 children were enrolled in this study. Inclusion criteria were as follows: 1) diagnosis of pneumonia; 2) nasopharyngeal aspirate (NPA) specimens collected for *M. pneumoniae* DNA detection after informed consent was obtained; 3) living in Hangzhou; and 4) age of less than 18 years. Pneumonia was defined by fever, respiratory symptoms (including cough, sputum, and shortness of breath), and parenchymal infiltrates shown on chest radiography. Children with pneumonia who had no NPA specimens collected for *M. pneumoniae* DNA detection were excluded. The study was approved by the Ethics Committee of Children's Hospital, Zhejiang University School of Medicine.

Detection of *M. pneumoniae*

NPA specimens of each patient with pneumonia were collected with a disposable sputum suction set with controlled pressure on the day of admission. *M. pneumoniae* DNA was detected by fluorescence quantitative real-time polymerase chain reaction (PCR) using a quantitative diagnostic kit for *M. pneumoniae* DNA (PCR fluorescence probing) (Da An Gene Co., Ltd. of Sun Yat-sen University, China) based on the TaqMan PCR.[9] Amplification, detection, and data analysis were carried out with an applied biosystems 7500 real-time PCR system (Applied Biosystems, Inc., CA, USA).

Meteorological data

Meteorological data in Hangzhou including air temperature (ºC), relative humidity (%), precipitation (mm), and raining days were obtained from the Hangzhou Meteorological Bureau. Temperature and humidity were read from a thermometer and a humidity meter respectively in instrument shelters 1.5 meters in height each hour. Daily precipitation was measured by a udometer. Readings were calculated into monthly mean value to coincide with the MPP data. A raining day is the day when daily precipitation is more than 0.1 mm.

Statistical analysis

Data analysis was primarily descriptive and was made using SPSS version 16.0 (SPSS Inc., USA). Multiple linear regression was used to analyze the relationship between meteorological factors and the positive rates of MPP (MPP rates). Proportions were compared using the chi-square test or Fisher's exact test. MPP rates in different age groups and years were compared using trend test. P value <0.05 was considered statistically significant.

Results

In the 14 799 children with pneumonia, 9509 were boys and 5290 were girls, with a male to female ratio of 1.8 (Table 1). *M. pneumoniae* DNA was positive in 2744 children (18.5%). Altogether, 1610 boys (16.9%) and 1134 (21.4%) girls were MPP positive; there was a statistical significant difference between both genders (χ^2=45.68, P<0.001).

The youngest child was 1 month old and the oldest was 17 years old, with a median of 6.9 months (25th-75th percentile: 2.4-21 months). In children younger than 1 year, 1-2 year, 3-6 years and older than 7 years, 944 (9.8%), 569 (21.1%), 727 (44.4%) and 504 (61.6%) were MPP positive, respectively (Table 1). MPP rate was higher in older children than in younger ones with an increasing tendency (trends test χ^2=46.72, P<0.001).

The number of *M. pneumoniae* positive cases in summer, autumn, spring, and winter was 693 (positive rate, 27.8%), 734 (23.9%), 682 (18.0%), and 635 (11.6%), respectively in a descending order (χ^2=372.75, P<0.001) (Fig. 1). In 2007, 2008, and 2009, the number of *M. pneumoniae* positive cases was 654 (12.9%), 935 (19.3%), and 1155 (23.6%), respectively, which showed an increasing tendency (trends test χ^2=13.72, P<0.001).

Table 1. Demographics of the 14 799 patients

Variables	*n* (%)
Male	9509 (64.3)
Female	5290 (35.7)
Male/female ratio	1.8
Age	
Younger than 1 y	944 (9.8)
1-2 y	569 (21.1)
3-6 y	727 (44.4)
Older than 7 y	504 (61.6)

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Monthly MPP rates and meteorological data are shown in Table 2. Of the meteorological data, only monthly mean air temperature was included in the model (*P*<0.001). The regression equation was MPP rate (%) = 5.875 + 0.830 × monthly mean air temperature (°C), which indicated that MPP rate increased by 0.830% with an increase of 1°C in monthly mean air temperature (Fig. 2). The other three meteorological factors including monthly mean relative humidity, monthly precipitation, and monthly raining

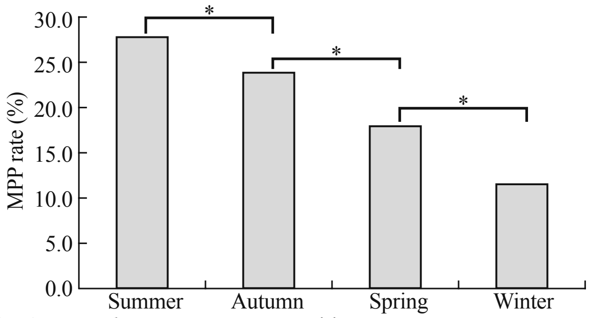

Fig. 1. *Mycoplasma pneumoniae* positive rates vary among seasons. *: *P*<0.05.

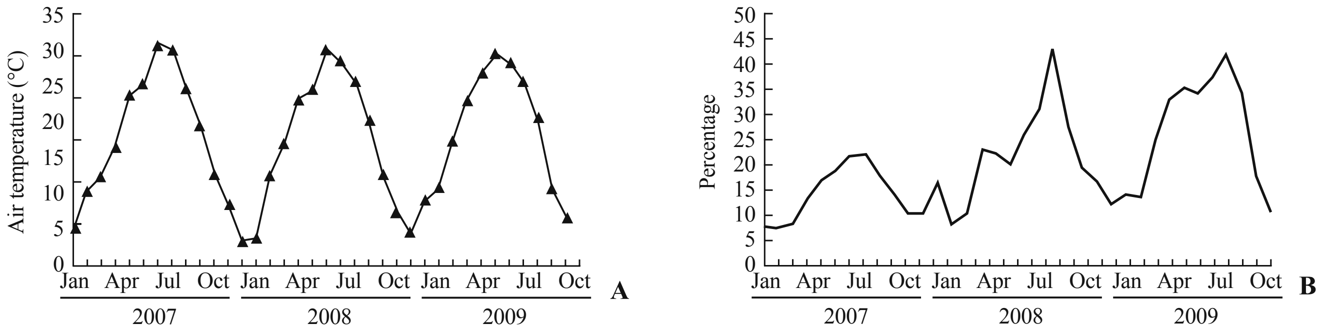

Fig. 2. Monthly mean air temperature influenced monthly *Mycoplasma pneumoniae* pneumonia rate. **A:** monthly mean air temperature (°C); **B:** *Mycoplasma pneumoniae* pneumonia rate (%).

Table 2. Monthly *Mycoplasma pneumoniae* positive rates and meteorological data from 2007 to 2009

Year	Month	Monthly *M. pneumoniae* positive rate (%)	Monthly mean air temperature (°C)	Monthly mean relative humidity (%)	Monthly precipitation (mm)	Monthly rain days
2007	Jan	7.9	5.3	73	82.8	15
	Feb	7.7	10.5	71	49.4	8
	Mar	8.9	12.7	72	171.3	11
	Apr	13.5	16.5	63	149.1	12
	May	17.1	23.8	65	32.8	11
	Jun	18.9	25.4	80	178.6	19
	Jul	22.0	30.9	67	122.7	9
	Aug	22.3	30.2	68	60.3	11
	Sept	18.1	24.6	77	215.9	15
	Oct	14.4	19.8	73	248.5	4
	Nov	10.6	12.9	70	31.5	6
	Dec	10.5	8.7	77	35.6	13
2008	Jan	16.6	3.7	75	91.7	16
	Feb	8.4	3.9	65	61.4	7
	Mar	10.4	12.7	64	37.7	8
	Apr	23.1	17.1	68	101.9	13
	May	22.3	23.2	62	117.7	9
	Jun	20.2	24.6	81	361.0	17
	Jul	25.8	30.1	69	114.4	12
	Aug	31.1	28.4	76	137.5	11
	Sept	43.0	25.8	76	44.2	9
	Oct	27.6	20.4	75	67.4	10
	Nov	19.6	12.9	72	118.5	12
	Dec	16.8	7.6	61	20.5	6
2009	Jan	12.3	4.4	65	36.3	10
	Feb	14.5	9.5	81	190.7	17
	Mar	13.6	11.1	74	117.6	15
	Apr	25.2	17.6	64	117.9	9
	May	33.1	22.9	59	77.0	10
	Jun	35.4	26.8	72	85.6	16
	Jul	34.2	29.6	69	227.7	9
	Aug	37.4	28.4	79	213.0	18
	Sept	41.8	25.5	76	113.7	11
	Oct	34.3	20.6	67	18.0	3
	Nov	18.1	10.8	79	186.6	14
	Dec	10.7	6.7	70	69.8	10

days were excluded from the model.

Discussion

The effect of gender on *M. pneumoniae* infection is different. Studies have found that gender is not an important factor for *M. pneumoniae* infection.[10-12] In our study, however, the positive rate of *M. pneumoniae* DNA was higher in girls than in boys.

Children of more than 7 years old in our study had the highest positive rate as reported elsewhere. In Turkey, serum specific IgG was positive only in children of more than 2 years old, with a sudden increase of seropositivity at 7 years and a peak at 10 years.[13] Similar sudden increase and peak were also reported in Japan.[14] In Australia, the age group most commonly affected by *M. pneumoniae* was those of 5-9 years old.[15] The outbreak of *M. pneumoniae* is closely related to contact types, e.g., schools, kindergartens, and militaries,[16] which could partially explain the age trend in the mentioned reports including ours. Some studies reported that most of patients with *M. pneumoniae* infection were younger than 5 years.[17] Interestingly, Phares et al[11] found that the incidence of *M. pneumoniae* was the highest in infants but the incidence of MPP in pneumonia caused by *M. pneumoniae*, *Legionella longbeachae*, *Chlamydia pneumoniae* was higher in children of more than 5 years old. In the present study, the MPP rate increased as the age of patients grew. This phenomenon may be partly due to the lower incidence of pneumonia caused by other agents in older children.

It is generally accepted that *M. pneumoniae* infection varies in frequency over the years, and a 3-4 year cycle was observed in North America, Europe, Japan and Australia.[2,14,15] In our study, however, MPP rates increased significantly from 2007 to 2009. We postulated that the period of our research was part of the cycle. Further observation is needed to confirm our notion.

In Hangzhou, the MPP rate was highest in summer and comparatively lower in autumn, spring and winter. Foy et al[5] found that *M. pneumoniae* infection was endemic without significant seasonal fluctuations in a 12-year study in Seattle and Washington. A study on both children and adults in Yugoslavia revealed that MPP was more frequent between August and November.[18] Another study found that *M. pneumoniae* infection was more common in winter than other seasons in Istanbul, Turkey.[6] A peak of *M. pneumoniae* infection in June or July was observed in Italy and Australia.[15,19] In a study conducted between 1986 and 2004 in Korea,[20] the earlier epidemics of *M. pneumoniae* infection up to 1996 peaked in summer, whereas the later epidemics peaked in autumn or early winter. However, the above data were all reported in different climate areas other than subtropical monsoon climate areas. In order to define more subtle factors influencing MPP, we further explored the effects of meteorological factors on MPP.

The present study revealed a strong positive correlation between *M. pneumoniae* positive rate and monthly mean air temperature. The survival of *M. pneumoniae* in aerosols was found to be best at an extremely low relative humidity. The temperature response was mediated by humidity.[21] The effects of temperature were such that irrespective of relative humidity, an increase in temperature resulted in a decreased airborne survival time in laboratory settings.[21] In real-life, Onozuka et al[8] found the number of cases of MPP increased with higher temperature or relative humidity in the weeks preceding disease onset which was opposite to the experimental results. Although humidity was thought to be an important factor for survival of *M. pneumoniae*,[8,21] our data proved no correlation between MPP rate and humidity or between temperature and humidity. Nor other meteorological factors including monthly mean precipitation and raining days were found to be correlated to the MPP rate.

There are shortcomings in the present study. First, the study period was not long enough. The epidemiological trend or the cyclical pattern was not fully observed. The relationship between epidemiological characteristics and meteorological factors was not elucidated. Second, the study was conducted only in one city. Large-scale epidemiological studies in other areas are needed to confirm the correlation between *M. pneumoniae* infection and meteorological factors. Third, control group was not set in the study. Fourth, more detailed clinical features such as laboratory data were not analyzed. However, the present study with its great number of enrolled patients provides useful information to pediatricians.

In conclusion, the MPP rate is higher in older children and it is highest in summer, followed by autumn, spring and winter in Hangzhou. The MPP rate is increased as monthly mean air temperature increases.

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Competing interest: None declared.

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Contributors: Xu YC proposed the study and wrote the first draft. Zhu LJ, Xu D, Tao XF, Li SX, Tang LF and Chen ZM collected and analyzed the data. All authors contributed to the design and interpretation of the study. Chen ZM is the guarantor.

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