Epidemiology and clinical features of segmental/lobar pattern *Mycoplasma pneumoniae* pneumonia: A ten-year retrospective clinical study

JIAN GAO[1*], BAOZHU YUE[1*], HAITAO LI[2], RONG CHEN[1], CHUNLIAN WU[1] and MILI XIAO[3]

[1]Department of Pediatrics, Weifang Maternal and Child Health Hospital; [2]Pulmonary Department, Weifang Chest Hospital, Weifang, Shandong 261011; [3]Department of Neonatology, Children's Hospital of Fudan University, Shanghai 201102, P.R. China

Abstract. *Mycoplasma pneumoniae* plays an important role in community-acquired pneumonia. However, epidemiological and clinical studies on the segmental/lobar pattern (S/L) radiographic-pathologic subtype of pediatric *Mycoplasma pneumoniae* pneumonia (MPP) are rare. The current study retrospectively analyzed the epidemiological and clinical characteristics of pediatric MPP patients. A total of 1,933 children with MPP received treatment at a single hospital between 2000 and 2009, of which 684 (35.4%) were diagnosed with S/L-MPP. The annual incidence of S/L-MPP in children with MPP increased throughout the duration of this study (from 6.4 to 59.6%, P<0.001), which was particularly evident after 2003. S/L-MPP was predominantly found in pre-school-aged children (4-6 years old; 56.6%). Compared with non-S/L-MPP, S/L-MPP was more closely associated with severe manifestations, including higher rates of fever (90.2 vs. 83.3%), pleural effusion (3.9 vs. 1.3%), extrapulmonary manifestations (26.2 vs. 21.2%), abnormal white blood cell counts (65.5 vs. 55.2%), abnormal C-reactive protein levels (30.9 vs. 23.7%) and bacterial co-infection (32.0 vs. 24.9%), as well as longer durations of fever (4.13±4.28 vs. 3.02±2.22 days) and hospitalization (12.70±4.54 vs. 9.22±5.12 days). Older S/L-MPP patients showed higher rates and longer durations of fever and cough; however, they also displayed a lower rate of extrapulmonary manifestations when compared with younger patients. In conclusion, the annual incidence of S/L-MPP has increased in recent years. Pre-school-aged children (4-6 years) with MPP are more likely to display a segmental/lobar pattern, which is associated with more severe clinical manifestations than other MPP infection patterns.

Introduction

Mycoplasma pneumoniae is responsible for 15-20% of all cases of community-acquired pneumonia (CAP) (1-3), which is the main cause of hospitalization and mortality in Chinese children (4). *M. pneumoniae* is a common cause of pneumonia in older children and adolescents (3,5-8); however, contrary to previous thought, the incidence of *M. pneumoniae* pneumonia (MPP) is also high among patients <1 year of age and among patients between 1 and 4 years of age (6-9).

The classical radiological presentations of MPP include lobar/segmental air-space consolidation and diffuse tiny centrilobular nodules and bronchovascular thickening (10-13). Previous studies have proposed that lobar alveolar consolidation is rare or infrequent in pediatric MPP patients (14,15). However, other reports have suggested that lobar consolidation may occur more frequently than was generally recognized (16,17). The lobar/segmental pattern is considered to account for 17-76.5% of pediatric MPP cases (6,16-19). Severe MPP often shows segmental or lobar infiltrates in one or more lobes (20), which, taken in the context of the estimated prevalence of MPP in pediatric patients, suggests that the lobar/segmental pattern is an important pathological category in pediatric MPP. However, large-scale, population-based epidemiological and clinical research studies analyzing segmental/lobar MPP remain rare.

In the present study, the epidemiological and clinical features of segmental/lobar pattern MPP were retrospectively analyzed in hospitalized children from 2000 to 2009 to improve the understanding of the prevalence and exploitable therapeutic characteristics of pediatric MPP.

Patients and methods

Patients. Weifang Maternal and Child Health Hospital is situated on the Shandong Peninsula in an eastern coastal area of China. This hospital serves as a primary source of healthcare

Correspondence to: Professor Jian Gao, Department of Pediatrics, Weifang Maternal and Child Health Hospital, 76 Qingnian Road, Weifang, Shandong 261011, P.R. China
E-mail: gaojian12319@163.com

*Contributed equally

for women, gravidae and children in Weifang. Weifang has a population of nine million, moderate economic development and stable infrastructure. In this study, a retrospective analysis of the medical records of children with pneumonia (as defined by the specifications in the International Classification of Diseases, 10th edition, ICD-10 code) who were admitted to Weifang Maternal & Child Health Hospital between January 2000 and December 2009 was conducted.

Patients who presented with clinical signs and symptoms of pneumonia underwent a chest radiograph, and the pneumonia pattern was characterized based on the World Health Organization Standardization of Interpretation of Chest Radiographs for the diagnosis of CAP in children (21). Patients diagnosed with pneumonia were included in this study if the chest radiographs were performed during hospitalization and serological *M. pneumoniae*-IgM and *M. pneumoniae* particles were detected by polymerase chain reaction (PCR) in naso-pharyngeal secretions ≥7 days following the onset of disease. Patients >14 years of age or suffering from known coexisting chronic, progressive or oncological illnesses were excluded from the analysis. Furthermore, based on chest radiographs, serological IgM tests and *M. pneumoniae* PCR tests, the patients were categorized into the following groups: i) lobar pneumonia (LP) if evidence of distinctive subsegmental, segmental or lobar consolidation was observed on the chest radiograph (20); ii) MPP if positive serological *M. pneumoniae* IgM and PCR tests from nasopharyngeal secretions were observed; iii) segmental/lobar pattern *M. pneumoniae* pneumonia (S/L-MPP) (20) if tests satisfied the criteria for LP and MPP, which is also characterized as air-space disease (10); and iv) non-segmental/lobar pattern *M. pneumoniae* pneumonia (non-S/L-MPP) if patients presented with MPP but did not fit the criteria for S/L-MPP. The non-S/L-MPP category included patients with pulmonary perihilar linear opacities or infiltrates or reticulonodular infiltrates by chest radiography, as well as patients with an interstitial and bronchial pattern of MPP.

A total of 18,739 patients with pneumonia were admitted during the period of study, of which 7,319 were enrolled in this study. Data were collected regarding age, gender, clinical signs and symptoms, laboratory and radiological findings, treatment, complications and duration of hospitalization. Microflora were also detected using nasopharyngeal swab or sputum specimens by culturing and processing in accordance with standard microbiological procedures. A qualitatively indirect serum agglutination assay based on the Gold-labeled Immunologic Filtration Assay (GIFA; Kanghua Biotech Co., Ltd., Weifang, China) was used to detect serological *M. pneumoniae* IgM (22,23).

The clinical features of the S/L-MPP patients were evaluated according to age in the following groups: ≤3 years of age (infants and young children), 4-6 years of age (pre-school-aged children), and ≥7 years of age (school-aged children). The clinical and laboratory findings were compared according to the pneumonia pattern. This study was approved by the Institutional Review Board of Weifang Maternal and Child Health Hospital, and written informed consent was obtained from the guardians of the patients.

Statistical analysis. Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows version 11.5 (SPSS, Inc., Chicago, IL, USA). Continuous variables are reported as the mean ± standard deviation. Since patient age may have an association with the levels of certain laboratory indices, including white blood cell count (WBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), these quantitative data were transformed into categorical data (normal or abnormal). Statistical significance was assessed using the Chi-square test or Fisher's exact test for categorical variables, and the *t*-test and one-way analysis of variation (ANOVA) for continuous variables. The trends in the annual incidences of LP, MPP and S/L-MPP were assessed using a trend test. P<0.05 was considered to indicate a statistically significant difference.

Results

Epidemiological characteristics. Of 18,739 children hospitalized with pneumonia from January 2000 to December 2009, 7,319 were enrolled in this study, of whom 4,282 were boys and 3,037 were girls, corresponding to a male to female ratio of 1.4:1. Of the 7,319 patients enrolled, 823 children (11.2%; 489 boys and 334 girls) were diagnosed with LP, 1,933 children (26.4%; 1,110 boys and 823 girls) were diagnosed with MPP, and 684 children (9.3%; 385 boys and 299 girls) were diagnosed with S/L-MPP.

The annual incidence rates of MPP, LP and S/L-MPP are displayed in Fig. 1. The annual incidence of MPP showed an overall increasing trend over the 10-year course of the study (P<0.001); the highest incidence was in 2008 (286/896 cases, 31.9%), and the lowest was in 2000 (85/502 cases, 16.9%). The annual incidence of LP and S/L-MPP showed an initial similarly increasing trend (P<0.001), which accelerated after 2005; the highest incidence for both diseases was in 2009 (22.9 and 16.2%, respectively), and the lowest incidence for both diseases was in 2002 (2.0 and 1.7%, respectively).

Among the 823 LP patients observed between 2000 and 2009, of which 83.1% were infected with *M. pneumoniae*; the highest annual incidence was in 2004 (36/38 cases, 94.7%), and the lowest incidence was in 2001 (9/14 cases, 64.3%). However, a decreasing trend (P=0.028) was observed after 2004 (P<0.001; Fig. 2).

Between 2000 and 2009, 1,933 patients were diagnosed with MPP, 35.4% of whom were further diagnosed with S/L-MPP. The highest annual incidence occurred in 2007 (165/277 cases, 59.6%), and the lowest incidence occurred in 2002 (10/157 cases, 6.4%). A significant upward trend was observed in the annual incidence of S/L-MPP in children with MPP (P<0.001), which is similar to that observed in children suffering from general pneumonia (Fig. 3).

The age of children with MPP ranged from 8 months to 14 years (mean, 6.74±4.12 years), and the age distribution is summarized in Table I. The age distribution in non-S/L-MPP patients was significantly different from the distribution observed in S/L-MPP patients (P<0.001). The incidence of S/L-MPP was higher in children aged 4-6 years (336/684 cases, 49.1%), whereas the incidence of non-S/L-MPP was higher in patients ≥7 years of age (819/1,249 cases, 65.6%).

Clinical and laboratory assessment according to pneumoniae pattern. Clinical data and the initial clinical assessment of the
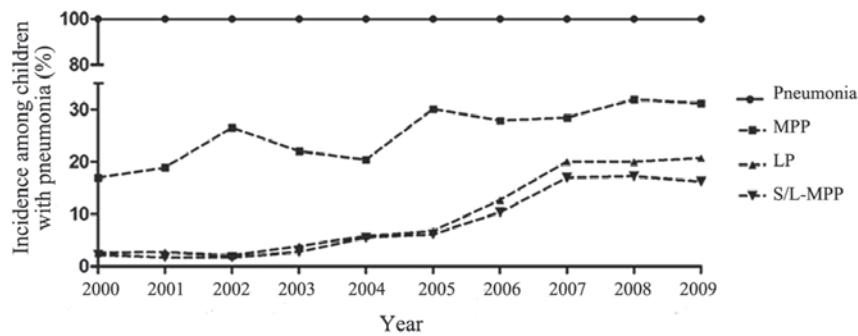
Figure 1. Annual incidence of MPP, LP and S/L-MPP in children with pneumonia. MPP, *Mycoplasms pneumoniae* pneumonia; LP, lobar pneumonia; S/L-MPP, segmental/lobar pattern *M. pneumoniae* pneumonia.
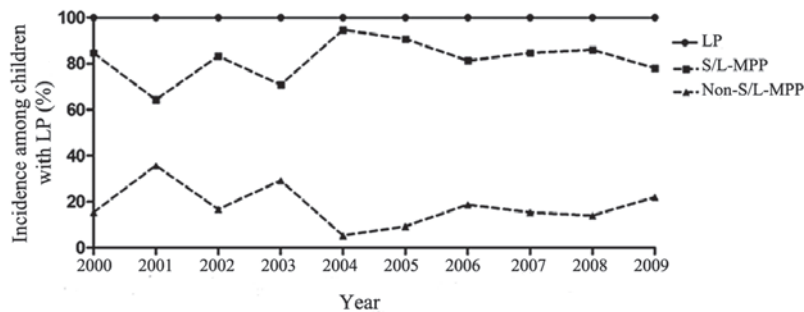

Figure 2. Annual incidence of S/L-MPP and non-S/L-MPP in children with LP. LP, lobar pneumonia; S/L-MPP, segmental/lobar pattern *Mycoplasma pneumoniae* pneumonia; non-S/L-MPP, non-segmental/lobar pattern *M. pneumoniae* pneumonia.
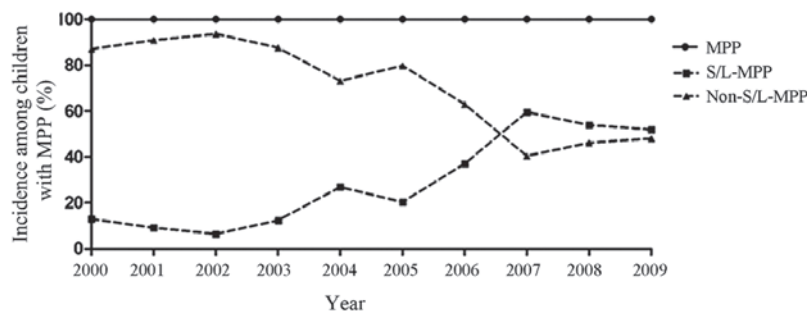

Figure 3. Annual incidence of S/L-MPP and non-S/L-MPP in children with MPP. MPP, *Mycoplasma pneumoniae* pneumonia; S/L-MPP, segmental/lobar pattern *M. pneumoniae* pneumonia; non-S/L-MPP, non-segmental/lobar pattern *M. pneumoniae* pneumonia.

children with MPP are presented in Table I. Relative to the children with non-S/L-MPP (1,041/1,249 cases, 83.3%), those with S/L-MPP (617/684 cases, 90.2%) had a higher rate of fever (P<0.001). Moreover, the duration of the fever for the S/L-MPP group (mean, 4.13±4.28 days) was significantly longer than that observed in the non-S/L-MPP group (mean, 3.02±2.22 days, P=0.028). Additionally, the duration of coughing was longer in the S/L-MPP group; however, this difference in duration was not found to be statistically significant (mean, 9.43±7.62 vs. 7.86±5.92 days, P=0.084). Extrapulmonary manifestations, including erythematous maculopapular rash, liver and kidney function lesions, and neurological complications, occurred in 444 MPP patients (22.3%). The results show that the incidence of extrapulmonary manifestations was significantly higher in children with S/L-MPP (179/684 cases, 26.2%) than in children with non-S/L-MPP (265/1,249 cases,

21.2%; P=0.013). The S/L-MPP group showed a higher rate of abnormal WBC counts (P<0.001) and CRP levels (P=0.002) relative to the non-S/L-MPP group. Nasopharyngeal swab or sputum specimen cultures detected pathogens in 1,174 MPP patients, and 326 (27.8%) of these patients were co-infected with bacteria, including *Klebsiella pneumoniae* (112 cases, 34.4%), *Streptococcus pneumoniae* (92 cases, 28.2%), *Escherichia coli* (67 cases, 20.5%), *Staphylococcus aureus* (30 cases, 9.3%) and other pathogenic bacteria (25 cases, 7.7%). The incidence of co-infection with bacteria was significantly higher in children with S/L-MPP (152/475 cases, 32.0%) than in those with non-S/L-MPP (174/699 cases, 24.9%; P=0.008; Table I).

Radiological imaging demonstrated that segmental/lobar consolidation was mainly located in the lower lung lobe (501 cases, 73.3%), of which 297 cases were located in the right

Table I. Clinical and treatment data of children with MPP (n=1,933).

Variables	No.	S/L-MPP (n=684)[a]	Non-S/L-MPP (n=1,249)[b]	P-value
Gender				0.454
Male	1,110	385	725	
Female	823	299	524	
Age (years)				<0.001
≤3	341	169	172	
4 to 6	594	336	258	
≥7	998	179	819	
Fever				<0.001
Yes	1,658	617	1,041	
No	275	67	208	
Duration of fever (days)	1,933	4.13±4.28	3.02±2.22	0.028
Duration of cough (days)	1,993	9.43±7.62	7.86±5.92	0.084
Gasping				0.555
Yes	499	182	317	
No	1,434	502	932	
Pulmonary crackles at onset				0.436
Yes	746	256	490	
No	1,187	428	759	
Pleural effusion				<0.001
Yes	43	27	16	
No	1,890	657	1,233	
Extrapulmonary manifestations				0.013
Yes	444	179	265	
No	1,489	505	984	
WBC				<0.001
Abnormal	1,137	448	689	
Normal	796	236	560	
ESR				0.697
Abnormal	236	87	149	
Normal	1,324	471	854	
CRP				0.002
Abnormal	381	176	205	
Normal	1,054	393	661	
Co-infection with bacteria				0.008
Yes	326	152	174	
No	848	323	525	
Sensitivity to macrolide antibiotics				0.197
Yes	1,860	653	1,207	
No	73	31	42	
Antibiotic-combination treatment				0.004
Yes	1,622	596	1,026	
No	311	88	223	
Duration of hospitalization (days)	1,933	12.70±4.54	9.22±5.12	0.032

[a]Excluding ESR (n=558), CRP (n=569) and bacterial co-infection (n=475); [b]excluding ESR (n=903), CRP (n=866) and bacterial co-infection (n=699) MPP, *Mycoplasma pneumoniae* pneumonia; S/L-MPP, segmental/lobar pattern *M. pneumoniae* pneumonia; non-S/L-MPP, non-segmental/lobar pattern *M. pneumoniae* pneumonia; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

lobe and 204 cases were in the left lobe (Fig. 4). The incidence of pleural effusion in children with S/L-MPP (27/684 cases, 3.9%) was significantly higher than that in children with non-S/L-MPP (16/1,249 cases, 1.3%; P<0.001).

Table II. Clinical data of children with S/L-MPP (n=684) according to age group.

Variables	No.	≤3 years (n=169)[a]	4-6 years (n=336)[b]	≥7 years (n=179)[c]	P-value
Gender					0.077
Male	385	92	179	114	
Female	299	77	157	65	
Fever					0.048
Yes	617	148	301	168	
No	67	21	35	11	
Duration of fever (days)	684	3.49±3.22	3.68±4.64	5.25±4.77	0.036[d]
Duration of cough (days)	684	8.11±4.67	9.34±5.03	9.78±7.23	0.040[d]
Gasping					0.075
Yes	182	52	90	40	
No	502	117	246	139	
Pulmonary crackles at onset					0.637
Yes	256	65	118	73	
No	428	104	218	106	
Pleural effusion					0.473
Yes	27	6	12	9	
No	657	163	324	170	
Extrapulmonary manifestation					0.017
Yes	179	54	88	37	
No	505	115	248	142	
WBC					0.076
Abnormal	448	122	217	109	
Normal	236	47	119	70	
ESR					0.867
Abnormal	87	19	50	18	
Normal	471	130	223	118	
CRP					0.242
Abnormal	176	46	78	52	
Normal	393	97	202	94	
Co-infection with bacteria	475				0.004
Yes	152	48	70	34	
No	323	59	167	97	
Duration of hospitalization (days)	684	12.83±5.63	12.52±7.72	11.32±8.65	>0.05[e]

[a]Excluding ESR (n=149), CRP (n=143) and bacterial co-infection (n=107); [b]excluding ESR (n=273), CRP (n=280) and bacterial co-infection (n=237); [c]excluding ESR (n=136), CRP (n=146) and bacterial co-infection (n=131) Comparison between the ≤3 years group and the ≥7 years group; [e]no significant differences among the three groups. S/L-MPP segmental/lobar pattern *Mycoplasma pneumoniae* pneumonia; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Therapeutic characteristics. The medical and curative characteristics of the 1,933 hospitalized children with MPP were analyzed. Seventy-three (3.8%) of the MPP cases were resistant to treatment with macrolide antibiotics. S/L-MPP macrolide-resistant cases (31/684 cases, 4.5%) were observed to be more prevalent than non-S/L-MPP macrolide-resistant cases (42/1,249 cases, 3.4%); however, this difference in prevalence was not found to be statistically significant (P=0.197). The rate of antibiotic-combination treatment for S/L-MPP patients (596/684 cases, 87.1%) was significantly higher than that of non-S/L-MPP patients (1,026/1,249 cases, 82.1%;

P=0.004). Furthermore, the duration of hospitalization was observed to be significantly longer for the patients in the S/L-MPP group (mean, 12.70±4.54 days) than for the patients in the non-S/L-MPP group (mean, 9.22±5.12 days, P=0.032; Table I).

Clinical and laboratory results according to age in S/L-MPP. The 684 children with S/L-MPP included in this analysis were divided into three groups according to age. The older patients showed a higher rate of fever (P=0.048) and a longer duration of fever (P=0.036) and cough (P=0.040). However, the
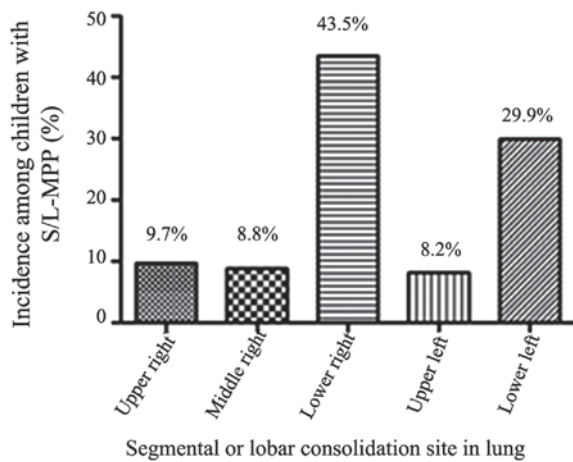
Figure 4. Incidences of various pulmonary segmental or lobar consolidation sites in children with S/L-MPP (n=684). S/L-MPP, segmental/lobar pattern *Mycoplasma pneumoniae* pneumonia.

older patients presented with a lower rate of extrapulmonary manifestations (P=0.017). Based on the laboratory findings, the younger patients had a higher rate of bacterial co-infection than the older patients (P=0.004; Table II).

Discussion

MPP has been extensively researched; however, systematic analysis of the epidemiological and clinical differentiation of the segmental/lobar pattern from the other radiographic patterns of pediatric MPP is rare. The present 10-year study analyzed children who were hospitalized and presented with the clinical features of S/L-MPP. The segmental/lobar pattern accounted for 35.4% of MPP patients and 83.1% of LP patients. Furthermore, pre-school children aged 4-6 years accounted for 56.6% of the segmental/lobar pattern cases. The annual incidence of S/L-MPP in children with MPP showed a rapidly increasing trend from 2000 to 2009. Compared with the non-segmental/lobar radiographic MPP pattern, S/L-MPP is associated with more severe clinical manifestations. The findings of the present study suggest that S/L-MPP plays a more significant role in MPP cases than was previously thought.

In this study, the mean prevalence of *M. pneumoniae* infection among children with pneumonia (26.4%) was similar to that in previous studies (3,5,24). Historically, endemic *M. pneumoniae* disease transmission has been punctuated with cyclic epidemics every 4-5 years (25,26). The results of the present study show a similar, albeit less evident, cycle from 2000 to 2009, which could be associated with differences in the region, time and detection methods of the study. The annual incidence of MPP showed a gradually increasing trend from 16.9 to 31.9% in this study, which is similar to that reported in other studies (27,28). The age distribution of MPP in the present study was also comparable to the age-related increase reported in the literature (1,5,7).

Generally, *M. pneumoniae* is considered an atypical bacterium that causes a form of CAP with radiological manifestations of interstitial lung disease and with a very slow and benign course (29). However, segmental/lobar consolidation has been suggested to occur more frequently in MPP than is

generally appreciated (16). Furthermore, segmental/lobar MPP has been shown to account for 17-76.5% of pediatric cases of MPP and has shown an increasing trend in incidence (6,16-19). In a study conducted in 1978 of 59 patients with documented *M. pneumoniae*, 20% were found to have a single homogeneous infiltrate that appeared as a bacterial lobar pneumonia (16). In another large urban survey conducted in 1980, lobar infiltrates were reported in 17% of MPP patients (19). Esposito *et al* reported that the lobar/segmental pattern occurred in 35.3% of MPP patients (2-12 years old) in 2001 (18). In a study conducted in 2004, Phares *et al* observed that 44% (38/85 cases) of MPP patients had alveolar consolidations (6). In 2008, Defilippi *et al* (17) reported that consolidations were the most frequent finding (76.5%, 62/76 cases) in chest X-rays of children with *M. pneumoniae* infection. Collectively, these studies indicate that the rate of lobar/segmental consolidation in MPP may be increasing each year. The data in the present study show that the incidence of segmental/lobar consolidation was 35.4% in children with MPP and 9.3% in those with pneumonia. The data also show that the annual incidence of S/L-MPP in children with MPP showed a rapidly increasing trend between 2000 and 2009, which was particularly evident after 2003. The highest incidence of S/L-MPP occurred in 2007 accounting for 59.6% of MPP cases and with a slight reduction observed after 2007. A gradual increase in the incidence of the segmental/lobar pattern suggests that severe MPP has increased in the most recent years of the present analysis. Moreover, the majority of LP patients (83.1%) were infected with *M. pneumoniae*; however, this trend showed a gradual reduction after 2004. The reasons for these observed trends are complex. Mixed infection (7,26,30) and macrolide-resistant (31,32) MPP have displayed altered trends in recent years. Liu *et al* reported that the rate of occurrence of macrolide-resistant *M. pneumoniae* was 83% (44/53 cases) between 2005 and 2008 (31) and increased to 90% in 2010 (32) in Shanghai, China. These time-related factors may be associated with the change in S/L-MPP incidence.

The data in the present study show that S/L-MPP predominantly occurs in pre-school-aged children (4-6 years old, 56.6%). *M. pneumoniae* is considered to be the primary causative agent of pneumonia in children aged 5-10 years (7) and has also been recognized as the primary causative agent of pneumonia in pre-school-aged children (27). Typically, an age-related increase in the incidence of pneumonia due to *M. pneumoniae* infection is observed (33,34). Additionally, Wu *et al* reported that in 1,009 children <18 years of age who were hospitalized for LP or pneumococcal pneumonia, 64% were <5 years of age; the age-specific incidence increased gradually and was highest in patients between 4 and 5 years of age, after which the incidence decreased yearly (35). In the present study, the age distribution of S/L-MPP intersected with that of MPP and LP, indicating that children <7 years of age with MPP could be more likely to present with an accompanying severe pulmonary lesion. This age distribution differs from that reported in a study conducted in Korea by Youn *et al* (20), in which the frequency of S/L-MPP was significantly higher in patients ≥6 years of age (69.1%) when compared with patients between 2 and 5 years of age (40.7%) or patients <2 years of age (20.7%). This difference in the age-specific incidence may be associated with differences

in age grouping, region, number of patients studied and the condition of the patients (particularly in older children).

The typical chest X-ray manifestation of MPP is a subsegmental patchy interstitial or alveolar (or both) infiltrate in one or more areas that occasionally occurs bilaterally (19). In the present study, it was observed that S/L-MPP is more often unilateral (86.5%) and confined to the lower lobes (73.3%, especially in the right), which differs from an earlier study on unilateral occurrence (35 and 50%) in the lower lobes (50.0%) (34). Pleural effusion is an unusual observation in MPP. In the present study, the incidence of pleural effusion among MPP patients (2.2%) was lower than that previously reported (5-20%) (34); however, the incidence in S/L-MPP patients (3.9%) was significantly higher than that of non-S/L-MPP patients (1.3%), suggesting that S/L-MPP is associated with more severe pulmonary lesions.

MPP is referred to as walking or atypical pneumonia, and the degree of consolidation may exceed what would be expected based on the severity of the clinical manifestations. Consistent with a previous study, the present study shows that relative to non-S/L-MPP, S/L-MPP is associated with more severe manifestations, including fevers of higher grade and longer duration, longer durations of cough, increased incidence of pleural effusion and additional extrapulmonary manifestations (20). Furthermore, it was found that younger children with S/L-MPP had a greater rate of febrile and extrapulmonary manifestations and a reduced duration of fever and cough. Anerythematous maculopapular rash was the most common extrapulmonary manifestation, whereas neurological complications were rare. These results suggest that S/L-MPP is associated with more severe clinical manifestations, particularly in younger children.

A clinical study has reported that children with S/L-MPP have significantly lower WBC and lymphocyte counts but higher CRP levels than children with bronchopneumonic patterns (20). However, consistent with another study, the present study shows that S/L-MPP is associated with higher rates of abnormal WBC counts and CRP levels than non-S/L-MPP (36). Furthermore, the increased rate of abnormal WBC counts (72.2%) may be associated with the increased febrile rate and co-infections in the younger patients. Co-infection with S. pneumoniae is present in >30% of M. pneumoniae CAP patients (27,30). In the present study, 27.8% of MPP patients were co-infected with another pathogen, and the most common co-infectious agent isolated was K. pneumoniae; however, S. pneumoniae has not been reported as a co-infectious agent (27). In the present study, S/L-MPP patients showed a higher rate of bacterial co-infection (32.0%) than non-S/L-MPP patients (24.9%), and this was particularly evident in children <3 years of age (44.9%). Extensive microbiological testing was not conducted, therefore the possibility that some children could have been co-infected with Chlamydia or a viral pathogen (27) cannot be excluded. Children with S/L-MPP in the present study had a longer duration of hospitalization and a higher rate of antibiotic combination therapy than those with non-S/L-MPP. Generally, lobar/segmental consolidation on chest radiographic findings is considered to be an air-space disease (10), which is a severe pathological manifestation in patients with MPP. Taking into account the severity of the illness, the antibiotic resistance patterns and comorbid conditions, empirical antibiotic combination therapy was relatively frequent in patients with S/L-MPP.

The limitations of this study include the fact that the study subjects only included those who were diagnosed with pneumonia by radiographic analysis, which is typically performed on patients with more severe clinical manifestations. The subjects enrolled in this study could have had more severe clinical and pathological manifestations than patients who do not typically undergo a chest X-ray, which may have contributed to a case-selection bias. Another limitation is the fact that M. pneumoniae cultures and serological PCR were unavailable; therefore, serological M. pneumoniae IgM and nasopharyngeal PCR may have produced false negative and false positive results.

In conclusion, it was found that a segmental/lobar pattern existed in 35.4% of MPP patients, and the annual incidence of S/L-MPP has increased in recent years. The incidence of S/L-MPP was the highest in pre-school children aged 4-6 years, in whom S/L-MPP presents with more severe clinical manifestations than non-S/L-MPP. With knowledge of these new epidemiological characteristics, clinicians are recommended to consider empirical antibiotic-combination treatment for MPP, particularly in pre-school-aged children.

References

1. Foy HM: Infections caused by *Mycoplasma pneumoniae* and possible carrier state in different populations of patients. Clin Infect Dis 17 (Suppl 1): S37-S46, 1993.
2. Marston BJ, Plouffe JF, File TM Jr, Hackman BA, Salstrom SJ, Lipman HB, Kolczak MS and Breiman RF; The Community-based Pneumonia Incidence Study Group: Incidence of community-acquired pneumonia requiring hospitalization: Results of a population-based active surveillance study in Ohio. Arch Intern Med 157: 1709-1718, 1997.
3. Waites KB and Talkington DF: *Mycoplasma pneumoniae* and its role as a human pathogen. Clin Microbiol Rev 17: 697-728, 2004.
4. Liu G, Talkington DF, Fields BS, Levine OS, Yang Y and Tondella ML: *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* in young children from China with community-acquired pneumonia. Diagn Microbiol Infect Dis 52: 7-14, 2005.
5. Heiskanen-Kosma T, Korppi M, Jokinen C, Kurki S, Heiskanen L, Juvonen H, Kallinen S, Stén M, Tarkiainen A, Rönnberg PR, *et al*: Etiology of childhood pneumonia: Serologic results of a prospective, population-based study. Pediatr Infect Dis J 17: 986-991, 1998.
6. Phares CR, Wangroongsarb P, Chantra S, Paveenkitiporn W, Tondella ML, Benson RF, Thacker WL, Fields BS, Moore MR, Fischer J, *et al*: Epidemiology of severe pneumonia caused by *Legionella longbeachae*, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*: 1-year, population-based surveillance for severe pneumonia in Thailand. Clin Infect Dis 45: e147-e155, 2007.
7. Korppi M, Heiskanen-Kosma T and Kleemola M: Incidence of community-acquired pneumonia in children caused by *Mycoplasma pneumoniae*: Serological results of a prospective, population-based study in primary health care. Respirology 9: 109-114, 2004.
8. Layani-Milon MP, Gras I, Valette M, Luciani J, Stagnara J, Aymard M and Lina B: Incidence of upper respiratory tract *Mycoplasma pneumoniae* infections among outpatients in Rône-Alpes, France, during five successive winter periods. J Clin Microbiol 37: 1721-1726, 1999.

9. Principi N and Esposito S: Emerging role of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in paediatric respiratory-tract infections. Lancet Infect Dis 1: 334-344, 2001.

10. John SD, Ramanathan J and Swischuk LE: Spectrum of clinical and radiographic findings in pediatric mycoplasma pneumonia. Radiographics 21: 121-131, 2001.

11. Nambu A, Saito A, Araki T, Ozawa K, Hiejima Y, Akao M, Ohki Z and Yamaguchi H: *Chlamydia pneumoniae*: Comparison with findings of *Mycoplasma pneumoniae* and *Streptococcus pneumoniae* at thin-section CT. Radiology 238: 330-338, 2006.

12. Reittner P, Muller NL, Heyneman L, Johkoh T, Park JS, Lee KS, Honda O and Tomiyama N: *Mycoplasma pneumoniae* pneumonia: Radiographic and high-resolution CT features in 28 patients. AJR Am J Roentgenol 174: 37-41, 2000.

13. Lee I, Kim TS and Yoon HK: *Mycoplasma pneumoniae* pneumonia: CT features in 16 patients. Eur Radiol 16: 719-725, 2006.

14. George RB, Weill H, Rasch JR, Mogabgab WJ and Ziskind MM: Roentgenographic appearance of viral and mycoplasmal pneumonias. Am Rev Respir Dis 96: 1144-1150, 1967.

15. Murray HW, Masur H, Senterfit LB and Roberts RB: The protean manifestations of *Mycoplasma pneumoniae* infection in adults. Am J Med 58: 229-242, 1975.

16. Brolin I and Wernstedt L: Radiographic appearance of mycoplasmal pneumonia. Scand J Respir Dis 59: 179-189, 1978.

17. Defilippi A, Silvestri M, Tacchella A, Giacchino R, Melioli G, Di Marco E, Cirillo C, Di Pietro P and Rossi GA: Epidemiology and clinical features of *Mycoplasma pneumoniae* infection in children. Respir Med 102: 1762-1768, 2008.

18. Esposito S, Blasi F, Bellini F, Allegra L and Principi N; Mowgli Study Group: *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* infections in children with pneumonia. Eur Respir J 17: 241-245, 2001.

19. Foy HM, Kenny GE, McMahan R, Mansy AM and Grayston JT: *Mycoplasma pneumoniae* pneumonia in an urban area. Five years of surveillance. JAMA 214: 1666-1672, 1970.

20. Youn YS, Lee KY, Hwang JY, Rhim JW, Kang JH, Lee JS and Kim JC: Difference of clinical features in childhood *Mycoplasma pneumoniae* pneumonia. BMC Pediatr 10: 48, 2010.

21. World Health Organization Pneumonia Vaccine Trial Investigators' Group. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children. http://apps.who.int/iris/bitstream/10665/66956/1/WHO_V_and_B_01.35.pdf. Accessed November 29, 2011.

22. Daxboeck F, Bauer CC, Assadian O and Stanek G: An unrecognized epidemic of *Mycoplasma pneumoniae* infection in Vienna. Wien Klin Wochenschr 118: 208-211, 2006.

23. Musatovova O, Kannan TR and Baseman JB: Genomic analysis reveals *Mycoplasma pneumoniae* repetitive element 1-mediated recombination in a clinical isolate. Infect Immun 76: 1639-1648, 2008.

24. Nolevaux G, Bessaci-Kabouya K, Villenet N, Andrèoletti L, Laplanche D, Carquin J, Abély M, De Champs C and Motte J: Epidemiological and clinical study of *Mycoplasma pneumoniae* respiratory infections in children hospitalized in a pediatric ward between 1999 and 2005 at the Reims University Hospital. Arch Pediatr 15: 1630-1636, 2008 (In French).

25. Hong JY, Nah SG, Nam SG, Choi EH, Park JY and Lee HJ: Occurrence of *Mycoplasma pneumoniae* pneumonia in Seoul, Korea, from 1986-1995. Korean J Pediatr 40: 607-613, 1997.

26. Kang KS and Woo HO: Pattern of occurrence of *Mycoplasma pneumoniae* pneumonia in admitted children, southern central Korea, from 1989 to 2002. Korean J Pediatr 46: 474-479, 2003.

27. Principi N, Esposito S, Blasi F and Allegra L; Mowgli Study Group: Role of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in children with community-acquired lower respiratory tract infections. Clin Infect Dis 32: 1281-1289, 2001.

28. Xu YC, Zhu LJ, Xu D, Tao XF, Li SX, Tang LF and Chen ZM: Epidemiological characteristics and meteorological factors of childhood *Mycoplasma pneumoniae* pneumonia in Hangzhou. World J Pediatr 7: 240-244, 2011.

29. Marrie TJ: Pneumococcal pneumonia: Epidemiology and clinical features. Semin Respir Infec 14: 227-236, 1999.

30. Toikka P, Juvén T, Virkki R, Leinonen M, Mertsola J and Ruuskanen O: *Streptococcus pneumoniae* and *Mycoplasma pneumoniae* coinfection in community acquired pneumonia. Arch Dis Child 83: 413-414, 2000.

31. Liu Y, Ye X, Zhang H, Xu X, Li W, Zhu D and Wang M: Antimicrobial susceptibility of *Mycoplasma pneumoniae* isolates and molecular analysis of macrolide-resistant strains from Shanghai, China. Antimicrob Agents Chemother 53: 2160-2162, 2009.

32. Liu Y, Ye X, Zhang H, Xu X, Li W, Zhu D and Wang M: Characterization of macrolide resistance in *Mycoplasma pneumoniae* isolated from children in Shanghai, China. Diagn Microbiol Infect Dis 67: 355-358, 2010.

33. Ito I, Ishida T, Osawa M, Arita M, Hashimoto T, Hongo T and Mishima M: Culturally verified *Mycoplasma pneumoniae* pneumonia in Japan: A long-term observation from 1979-99. Epidemiol Infect 127: 365-367, 2001.

34. Othman N, Isaacs D and Kesson A: *Mycoplasma pneumoniae* infections in Australian children. J Paediatr Child Health 41: 671-676, 2005.

35. Wu PS, Huang LM, Chang IS, Lu CY, Shao PL, Tsai FY and Chang LY: The epidemiology of hospitalized children with pneumococcal/lobar pneumonia and empyema from 1997 to 2004 in Taiwan. Eur J Pediatr 169: 861-866, 2010.

36. Cockcroft DW and Stilwell GA: Lobar pneumonia caused by *Mycoplasma pneumoniae*. Can Med Assoc J 124: 1463-1468, 1981.