Etiological profile and clinical characteristics of segmental/lobar pattern pneumonia in hospitalized children

CURRENT STATUS: POSTED

Wang Yanxia
Zibo Central Hospital

Ma Liji
Zibo Central Hospital

Li Ying
Zibo Central Hospital

Yuyun Li zbzxyyek@163.com
Zibo Central Hospital
Corresponding Author

Yanfei Zheng
Zibo Central Hospital

Xiaoyue Zhang
Zibo Central Hospital

DOI:
10.21203/rs.2.13231/v1

SUBJECT AREAS
Pediatrics

KEYWORDS
etiological profile; clinical characteristics; pathogen; segmental/lobar pattern pneumonia; mycoplasma pneumoniae;
Abstract

The occurrence of segmental/lobar pattern pneumonia in children increases with years recently. The pathogens of the disease may change for the abuse of antibiotics and the application of pneumococcal vaccines. The pathogens of segmental/lobar pattern pneumonia in hospitalized children and their association with clinical characteristics are poorly understood nowadays. The current study retrospectively analyzed the pathogens and clinical characteristics of segmental/lobar pattern pneumonia in children at a single hospital between 1st Jan 2014 and 31st Dec 2018. The pathogens and their associations with clinical characteristics were statistically analyzed. A total of 593 children with segmental/lobar pattern pneumonia received treatment at a single hospital during the study period. 451 patients were positive for one pathogen and 83 patients were positive for two pathogens or more. Mycoplasma pneumoniae (M.pneumoniae) (72.34%) was the most commonly detected pathogen, followed by streptococcus pneumoniae (S.pneumoniae) (8.77%). The infection of M.pneumoniae in children with segmental/lobar pattern pneumonia increased with years ($p<0.05$). The positive rate of M.pneumoniae increased with ages of patients ($p<0.05$). M.pneumoniae was statistically associated to the extrapulmonary manifestations while S.pneumoniae was statistically associated with abnormal WBCs and CRPs ($p<0.05$). In a summary, M.pneumoniae was the most positive pathogen of segmental/lobar pattern pneumonia in hospitalized children. The positive rate of M.pneumoniae in children with segmental/lobar pattern pneumonia increased with years and the ages of children. M.pneumoniae was associated with extrapulmonary manifestations while S.pneumoniae was associated with abnormal WBCs and CRPs.

Introduction

Community-acquired pneumonia (CAP) is one of the most common respiratory disorders in
children, which often needs hospitalization\textsuperscript{1}. Segmental/lobar pattern pneumonia is one of the common CAPs based on chest radiological findings of consolidation. Patients with segmental/lobar pattern pneumonia often suffer from cough, fever, and even serious complications such as pulmonary necrosis, pulmonary atelectasis, pulmonary consolidation and respiratory failure, increasing the rate of morbidity, mortality as well as the cost of health care in our society. However, the pathogens profile of segmental/lobar pattern pneumonia in hospitalized children has not been ever reported and it may vary with regions, times, antibiotics use, vaccines and so on. The detection of pathogens often needs several hours or even days. So doctors have to treat patients with antibiotics on experiences usually, which may cause improper use of antibiotics, prolong the suffering of patients and cause more sequelae. Therefore it was important to figure out the pathogens profile of segmental/lobar pattern pneumonia in hospitalized children and their associations with clinical characteristics.

The occurrence of segmental/lobar pattern pneumonia in hospitalized children increases with years clinically, which has drawn the great attention of patients and doctors. In this research, the pathogens of segmental/lobar pattern pneumonia and their clinical characteristics were retrospectively analyzed in children who were hospitalized in Zibo Central Hospital during 1\textsuperscript{st} Jan 2014 and 31\textsuperscript{st} Dec 2018 as follows.

**Patients And Methods**

**Including and excluding criteria**

Zibo city is located in the central of Shandong Province in China. Zibo Central hospital serves as a primary source of healthcare for about six million people in the area, which has moderate economic development and stable infrastructure. In the study, a retrospective review of the medical records from children with pneumonia (as defined by
the specifications in the International Classification of Diseases, 10th edition, ICD-10 code) who were admitted to Zibo Central Hospital between 1st Jan 2014 and 31st Dec 2018 was conducted.

Patients who presented with clinical signs and symptoms of pneumonia underwent a chest radiograph during hospitalization. The pneumonia pattern was characterized based on the World Health Organization Standardization of Interpretation of Chest Radiographs for the diagnosis of CAP in children. Two experienced pediatric radiologists evaluated chest Radiographs independently and agreed on the conclusion. Patients diagnosed with pneumonia were included in this study if the serological test of pathogens were detected ≥7 days following the onset of the disease and the chest radiographs showed segmental/lobar pattern pneumonia. Patients with pulmonary perihilar linear opacities or infiltrates or reticulonodular infiltrates by chest radiography were excluded. Patients >14 years old or suffering from known coexisting chronic, progressive or oncological illnesses were also excluded from the analysis.

A total of 9342 patients with pneumonia were admitted during the study period, of which 593 patients with segmental/lobar pattern pneumonia were included in this study. Data were collected regarding age, gender, clinical signs and symptoms, laboratory and radiological findings, complications and duration of hospitalization. Microflora was also detected using blood or sputum specimens by culturing and processing in accordance with standard microbiological procedures.

Statistical analysis.

Statistical analyses were performed using the Statistical package for the Social Science for Windows version 11.5 (SPSS, Inc., Chicago, IL, USA). Continuous variables were reported as the mean ± standard deviation. The levels of certain laboratory indices
including white blood cell counts (WBCs), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may have an association with ages of patients, so these quantitative data were transformed into categorical data (normal or abnormal). Statistical significance was assessed using the Chi-square test for categorical variables and the t-test for continuous variables. P<0.05 was considered to indicate a statistically significant difference.

Results

Overview of patients

Of 9342 children hospitalized with pneumonia from 1st Jan 2014 to 31st Dec 2018, 593 patients with S/L-PP consisting of 398 boys and 195 girls were included in this study. The male to female ratio was about 2:1. The age of the patients with S/L-PP ranged from 1 year to 13 years (7.4±3.1years). The number of patients with S/L-PP each year was 86, 98,115,137 and 157 respectively during the study period. The annual incidence of children with S/L-PP increased with years over the study period (P<0.05). The duration of fever and cough were 4.6±2.1 days and 10.6±8.7 days respectively. 169 patients had a gasping and 208 patients had pulmonary crackles at onset. There were 149 patients with extrapulmonary manifestations including erythematous maculopapular rash, liver and kidney function lesions, and neurological complications. Only a few patients had pleural effusion. There were 383 patients with abnormal WBCs, 69 patients with abnormal ESR and 148 patients with abnormal CRP. The duration of hospital stay was 15.5±3.1 days.

Pathogen distribution with years

Table.1 summarized the distribution of pathogens with years including M. pneumoniae, respiratory syncytial virus (RSV), chlamydia pneumonia (CP), influenza A virus (IFA), parainfluenza virus (PIVS), adenovirus (ADV), Q fever Coxiella (COX), Legionella
pneumophila (LP), influenza B virus (IFB), S.pneumoniae, Staphylococcus aureus (S. aureus), Pseudomonas aeruginosa (P.aeruginosa), Escherichia coli (E.coli), Klebsiella pneumoniae (K.pneumoniae), and so on. The positive rate of M.pneumoniae increased with years. The number of patients infected by M.pneumoniae was 43, 67, 96, 106, and 117 each year respectively. There were significant differences in the positive rate of M.pneumoniae between the groups divided by years of patients (p<0.05). But no significant differences were found in the positive rate for other pathogens between the groups.

**Age distribution of pathogens**

Table.2 summarized the distribution of pathogens with age group and showed that the positive rate of M.pneumoniae increased with ages. Significant differences were observed in the positive rate of M.pneumoniae between the age groups (p<0.05). However, no significant differences were found in the positive rate of other pathogens between the age groups.

**Sex distribution of pathogens**

Significant differences were not observed for M. pneumoniae and S.pneumoniae between male patients and female patients. 18 patients were positive for IFB including 6 male patients and 12 female patients. Female patients displayed significantly higher positive rate for IFB than male ones. No significant difference was observed for the other pathogens between sex groups.

**Season distribution of pathogens**

In general, the seasonality profile of each individual pathogen was diverse. However, we did not observe distinct patterns for the pathogens.

**Mixed infection types of pathogens**

Co-infections with multiple pathogens were common. There were 91 patients in whom 2 or
more pathogens were positive, representing 15.34% of the patients, and the types of co-infection were complex. These data indicated that 27.40% of the children with M. pneumonias infections were co-infected with other pathogens. A total of 15 patients showed infection with 3 pathogens or more. (Table.3)

**Association between pathogens and patients’ demographic and clinical characteristics**

Table.4 summarized the patients’ demographic and clinical information found in association with pathogen infections. The patients groups were divided according to pathogens. Patients with co-infections of pathogens were excluded. Since the sample size was too small to obtain significance in some statistical analyses, only M. pneumonias and S. pneumonias were included in the statistical analyses. M. pneumonias was statistically related to the extrapulmonary manifestations. S. pneumonias was statistically associated with abnormal WBCs and CRPs. (Table.5)

**Discussion**

Segmental/lobar pattern pneumonia, one kind of the community-acquired pneumonias (CAP), is a common pediatric low respiratory tract infection\(^3\). The increasing incidence of segmental/lobar pattern pneumonia with extensive alveolar infiltrates has been noted over the years. Currently therapeutic strategies on pediatric segmental/lobar pattern pneumonia are not standardized\(^3\). Although new antibiotics are developed increasingly, the morbidity and mortality of segmental/lobar pattern pneumonia have not met a marked fall. Generally, the patients with segmental/lobar pattern pneumonia often have more severe symptoms than those with no segmental/lobar pattern pneumonia. Segmental/lobar pattern pneumonia was more closely associated with severe manifestations, including higher rates of fever, pleural effusion, extrapulmonary manifestations, abnormal WBCs,
abnormal CRP and bacterial co-infection, as well as longer durations of fever and hospitalization\textsuperscript{4}. In our research, the duration of fever and hospitalization of the patients with segmental/lobar pattern pneumonia were 4.6±2.1 days and 15.5±3.1 days, which were similar to the previous report\textsuperscript{4}. However, the pathogens distribution of the disease and their association with clinical characteristics in children has not ever been found to be reported. Isolation of microbes is slightly difficult in children with segmental/lobar pattern pneumonia due to the difficulties in sputum expectoration and low positive rate of blood culture\textsuperscript{5}. Some detection may be positive about a week after the onset of the disease. Therefore, the treatment of the disease based on knowledge and experience is very important. This research described the pathogens and their association with clinical characteristics in the patients with segmental/lobar pattern pneumonia, which can add knowledge and experience of the disease for doctors.

The positive rate of the pathogens in patients with segmental/lobar pattern pneumonia was highly diverse in this research. M. pneumoniae was the most commonly detected pathogen. The total positive rate of M. pneumoniae was 72.34\% (429/593). M. pneumoniae infection increased with years. That suggested M. pneumoniae has become the main pathogen of the disease nowadays. It was different from the previous report\textsuperscript{6-7}. In fact, M. pneumoniae is an important cause of respiratory tract infections, and are estimated to be accountable for up to 30-40\% of CAP\textsuperscript{8-11}. The classical radiological presentations of M. pneumoniae pneumonia include segmental/lobar air-space consolidation and diffuse tiny centrilobular nodules and bronchovascular thickening\textsuperscript{12-15}. The segmental/lobar pattern pneumonia is considered to account for 17-76.5\% of pediatric M. pneumoniae pneumonia cases and shown an increasing trend in incidence\textsuperscript{16-19}. So M. pneumoniae has drawn the great attention of clinical doctors and patients. However, there
has been no any type of vaccines approved for use against M. pneumoniae now\textsuperscript{20}. The positive rate of M. pneumoniae in patients with segmental/lobar pattern pneumonia increased with ages of children. However, there have been no well reasons found for the phenomenon. It was postulated with 2 explanations. First, old patients prefer social activity in herd and chances for them to be infected were high. Second, the progression of the immune system in the patients was different between old children and young ones. A report suggested that M. pneumoniae pneumonia was closely correlated with the immune system of the patients\textsuperscript{20}. The different progression state of the immune system between old patients and young ones may be related with the different positive rate of M. pneumoniae in the patients. The positive rate of M. pneumoniae in male patients was not statistically different from female ones, which suggested that M. pneumoniae infection was not affected by sex ratio. The patients with segmental/lobar pattern pneumonia infected by M. pneumoniae occurred all the year round and didn’t vary with the change of seasons. The extrapulmonary complications in patients with segmental/lobar pattern pneumonia infected by M. pneumoniae were common and the prevalence rate may be up to 26.17 \textsuperscript{4}, which was similar to the results in this research. However the extrapulmonary complications occurred few in patients infected by other pathogens and was not discussed in the research.

The second positive rate of pathogen in patients with segmental/lobar pattern pneumonia was S.pneumoniae and it was 8\% in the research. The positive rate of S.pneumoniae was much lower than that of M. pneumoniae, which was different from the previous understanding\textsuperscript{6-7}. It was associated with the wide application of S.pneumoniae vaccines in China, which can prohibit the prevalence of S.pneumoniae infection\textsuperscript{21-24}. The abuse of antibiotics was common in the nationwide, which can also cut down the infection of
S.pneumoniae. The germ culture was a low positive method. And samples used for germ culture were usually taken after the patients had taken oral or intravenous antibiotics, which was another reason for the low positive rate of S.pneumoniae in the study. Compared with other pathogens, S.pneumoniae was significantly associated with abnormal WBCs and CRP, which may be used for the determination of segmental/lobar pattern pneumonia pathogens in clinical practice. But it should be studied further. However, M.pneumoniae and S.pneumoniae in children with lobar pneumonia counted for 81.1% of the pathogens in total, which was much higher than that reported by Saraya T\textsuperscript{25}. Other pathogens had low positive rate in this research, which was not discussed here. Some patients were infected by two or more pathogens in the research. Two pathogens co-infection type was the most common one. The common co-infection type of two pathogens was M. pneumoniae and S.pneumoniae. The co-infection of 3 pathogens or more was less. The association between co-infection of pathogens and their clinical characteristics were not further discussed here for small cases.

The study is also associated with some limitations. First, clinical data were retrospectively collected based on medical records, and therefore there may have been some selection bias. Second, the sample size was not sufficiently large to obtain significance in some statistical analyses. Third, some pathogens may not be found due to the limitation of the detection method.

In a summary, M. pneumoniae was the most important pathogen in the children with segmental/lobar pattern pneumonia. The prevalence of M. pneumoniae infection increased with years and ages of children. Old patients are more prone to be infected by M. pneumoniae. M. pneumoniae was associated with extrapulmonary manifestation while S.pneumoniae was associated with abnormal WBCs and CRP.
Declarations

Acknowledgements
We thank the hospital pediatricians and clinical teams on all the pediatric wards who provide care to the children.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors’ contributions
Li yuyun and Wang yanxia conceptualized the study. Li yuyun and Wang yanxia were responsible for data curation, formal analysis and wrote the original draft. Ma liji, Li ying, Zheng yanfei and Zhang xiaoyue were responsible for resources, supervision, validation and visualization. All authors read and approved the final manuscript.

Ethical statement and consent to participate
This study was approved by the Institutional Ethical Review Board of Zibo Central Hospital. Written informed consent was obtained from the guardians of the patients.

Patients consent for publication
Written informed consent for the publication was obtained from the guardians of the patients.

Conflicts of interest
The authors declare no conflict of interest.

References
1. Sinaniotis CA, Sinaniotis AC. Community-acquired pneumonia in children. Curr Opin Pulm Med 2005; 11: 218-225.
2. 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.

3. Mannu GS, Loke YK, Curtain JP, Pelpola KN, Myint PK. Prognosis of multi-lobar pneumonia in community-acquired pneumonia: a systematic review and meta-analysis. Eur J Internal Med 2013; 24: 857-863.

4. Gao J, Yeu B, Li H, Chen R, Wu C, Xiao M. Epidemiology and clinical features of segmental/lobar pattern Mycoplasma pneumoniae pneumonia: A ten-year retrospective clinical study. Exp Ther Med 2015; 10: 2337-2344.

5. Defilippi A, Silvestri M, Tacchella A, et al. Epidemiology and clinical features of Mycoplasma pneumoniae infection in children. Respir Med 2008; 102:1762-1768.

6. Rai P, Parrish M, Tay IJ, et al. Streptococcus pneumoniae secretes hydrogen peroxide leading to DNA damage and apoptosis in lung cells. Proc Natl Acad Sci UAS 2015; 112:E3421-3430.

7. Simell B, Auranen K, Kayhty H, et al. The fundamental link between pneumococcal carriage and disease. Exp Rev Vaccines 2012; 11:841-855.

8. Waites KB. New concepts of Mycoplasma pneumoniae infections in children. Pediatr Pulmonol 2003; 36:267-278.

9. Hornstleth A. [The virology of acute respiratory tract infections. 1. A survey on the etiology in children]. Ugeskr Laeger 1967; 129: 1253-1258.

10. Hornstleth A. [The virology of acute respiratory tract infections. 2. Isolation of viruses in hospitalized children]. Ugeskr Laeger 1967; 129: 1259-1265.

11. Harris M, Clark J, Coote N, et al. British Thoracic Society guidelines for the management of community-acquired pneumonia in children: update 2011. Thorax
12. John SD, Ramanathan J, Swischuk LE. Spectrum of clinical and radiographic findings in pediatric mycoplasma pneumonia. Radiographics 2001; 21:121-131.

13. Nambu A, Saita A, Araki T, et al. Chlamydia pneumoniae: Comparison with findings of Mycoplasma pneumoniae and Streptococcus pneumoniae at thin-section CT. Radiology 2006; 238(1):330-338.

14. Reittner P, Muller NL, Heyneman L, et al. Mycoplasma pneumoniae pneumonia: Radiographic and high-resolution CT features in 28 patients. AJR Am J Roentgenol 2000; 174:37-41.

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

16. Phares CR, Wangroongsarb P, Chantra S, 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 2007; 45: e147-e155.

17. Brolin I, Wernstedt L. Radiographic appearance of mycoplasma pneumonia. Scand J Respir Dis 1978; 59: 179-189.

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

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

20. Waites KB, Talkington DF. Mycoplasma pneumoniae and its role as a human pathogen. Clin Microbiol Rev 2004; 17:697-728.

21. Chen K, Zhang X, Shan W, Zhao G, Zhang T. Serotype distribution of Streptococcus
pneumoniae and potential impact of pneumococcal conjugate vaccines in China: A systematic review and meta-analysis. Hum Vaccin Immunother 2018; 14: 1453-1463.

22. Wang Y, Li J, Wang Y, Gu W, Zhu F. Effectiveness and practical uses of 23-valent pneumococcal polysaccharide vaccine in healthy and special populations. Hum Vaccin Immunother 2018; 14: 1003-1012.

23. Li R, Fan KX, Young M Jr, et al. Long-term antibody persistence study (3 years after last dose) of the 7-valent pneumococcal conjugate vaccine in young children in China. Vaccine 2016; 34: 5359-5365.

24. Che D, Zhou H, He J, Wu B. Modeling the impact of the 7-valent pneumococcal conjugate vaccine in Chinese infants: an economic analysis of a compulsory vaccination. BMC Health Serv Res 2014; 14: 56.

25. Saraya T. The history of Mycoplasma pneumoniae pneumonia. Front Microbiol 2016; 7:364.

Tables

Table 1. Pathogen distribution with years in patients with segmental/lobar pattern pneumonia

| year | 2014 | 2015 | 2016 | 2017 | 2018 | X2 | p   |
|------|------|------|------|------|------|----|-----|
| n    |      |      |      |      |      |    |     |
| M.pneumoniae | 43   | 67   | 96   | 106  | 117  | 31.46 | <0.01 |
| RSV  | 5    | 4    | 5    | 3    | 3    | 3.68 | >0.05 |
| CP   | 4    | 4    | 4    | 2    | 2    | 4.24 | >0.05 |
| IFA  | 4    | 1    | 3    | 3    | 2    | 3.76 | >0.05 |
| PIVS | 6    | 5    | 5    | 6    | 4    | 2.76 | >0.05 |
| ADV  | 5    | 5    | 4    | 4    | 2    | 4.68 | >0.05 |
| COX  | 4    | 5    | 5    | 4    | 4    | 1.71 | >0.05 |
| LP   | 3    | 3    | 4    | 1    | 1    | 5.37 | >0.05 |
| IFB  | 4    | 4    | 2    | 4    | 3    | 2.54 | >0.05 |
| S.pneumoniae | 11   | 10   | 10   | 11   | 10   | 3.22 | >0.05 |

Table 2. Age distribution of pathogens in patients with segmental/lobar pattern pneumonia
| age   | age<3year | 3≤age6 | 6≤age9 | 9≤age14 | X2  | p   |
|-------|-----------|--------|--------|---------|-----|-----|
| n     | 81        | 108    | 169    | 235     |     |     |
| M.pneumoniae | 45    | 67     | 128    | 189     | 25.79 | <0.01|
| RSV   | 5         | 4      | 5      | 6       | 2.56 | >0.05|
| CP    | 2         | 5      | 2      | 7       | 3.10 | >0.05|
| IFA   | 2         | 2      | 2      | 7       | 1.57 | >0.05|
| PIVS  | 2         | 5      | 10     | 9       | 1.84 | >0.05|
| ADV   | 6         | 2      | 7      | 4       | 7.44 | >0.05|
| COX   | 3         | 3      | 6      | 11      | 0.81 | >0.05|
| LP    | 2         | 3      | 2      | 5       | 1.01 | >0.05|
| IFB   | 5         | 3      | 3      | 7       | 3.65 | >0.05|
| S.pneumoniae | 7     | 9      | 17     | 19      | 0.73 | >0.05|

Table.3. Mixed infection types of pathogens
| Co-infection type                           | number |
|--------------------------------------------|--------|
| 2 pathogens                                | 76     |
| M.pneumoniae + RSV                         | 5      |
| M.pneumoniae + CP                          | 4      |
| M.pneumoniae + IFA                         | 4      |
| M.pneumoniae + PIVS                        | 7      |
| M.pneumoniae + ADV                         | 4      |
| M.pneumoniae + COX                         | 10     |
| M.pneumoniae + LP                          | 4      |
| M.pneumoniae + IFB                         | 6      |
| M.pneumoniae + S. pneumoniae               | 20     |
| M.pneumoniae + S. aureus                   | 2      |
| M.pneumoniae + K. pneumoniae               | 1      |
| M.pneumoniae + E.coli                      | 1      |
| RSV + CP                                   | 1      |
| RSV + E.coli                               | 1      |
| CP + IFA                                   | 1      |
| CP + PIVS                                  | 1      |
| CP + ADV                                   | 1      |
| CP + S. pneumoniae                         | 1      |
| IFA + LP                                   | 1      |
| COX + LP                                   | 1      |
| 3                                          | 14     |
| M. pneumoniae + CP + ADV                   | 1      |
| RSV + LP + IFB                             | 1      |
| PIVS + ADV + COX                           | 1      |
| M. pneumoniae + PIVS + ADV                 | 1      |
| M. pneumoniae + CP + S. pneumoniae         | 1      |
| M. pneumoniae + RSV + LP                   | 1      |
| M. pneumoniae + CP + IFA                   | 1      |
| M. pneumoniae + ADV + IFB                  | 1      |
| M. pneumoniae + PIVS + COX                 | 1      |
| M. pneumoniae + LP + S. pneumoniae         | 1      |
| M. pneumoniae + IFA + P. aeruginosa        | 1      |
| M. pneumoniae + ADV + COX                  | 1      |
| M. pneumoniae + RSV + CP                   | 1      |
| M. pneumoniae + IFA + COX                  | 1      |
| 4                                          | 1      |
| M. pneumoniae + IFA + ADV + COX            | 1      |
### Table 4. Association between pathogens and patients’ demographic and clinical characteristics

| variables                      | M.pneumoniae | RSV | CP | IFA | PIVS | ADV | COX | LP | IFB | S.pneumoniae |
|-------------------------------|--------------|-----|----|-----|------|-----|-----|----|-----|--------------|
| N                             | 353          | 11  | 7  | 3   | 14   | 8   | 6   | 4  | 8   | 28           |
| gender                        |              |     |    |     |      |     |     |    |     |              |
| male                          | 246          | 10  | 3  | 3   | 10   | 4   | 3   | 2  | 4   | 20           |
| female                        | 107          | 1   | 4  | 0   | 4    | 3   | 2   | 2  | 4   | 8            |
| age                           | 7.8±4.1      | 8.4±3.1 | 10.2±2.6 | 5.4±3.2 | 6.5±5.2 | 6.8±4.5 | 7.6±3.8 | 8.3±5.2 | 6.8±3.9 | 7.9±3.5      |
| fever                         |              |     |    |     |      |     |     |    |     |              |
| yes                           | 302          | 8   | 5  | 3   | 10   | 7   | 4   | 3  | 6   | 21           |
| no                            | 51           | 3   | 2  | 0   | 4    | 1   | 1   | 1  | 2   | 7            |
| Duration of fever(days)       | 4.9±2.8      | 5.7±3.2 | 3.5±2.6 | 4.3±3.2 | 3.8±2.3 | 4.5±1.9 | 5.6±2.4 | 4.1±2.4 | 4.7±2.6 | 4.5±2.4      |
| Duration of cough(days)       | 10.2±6.2     | 8.6±5.8 | 13.6±6.5 | 10.3±6.9 | 11.8±9.3 | 8.9±4.3 | 10.1±6.8 | 8.2±4.3 | 9.4±7.6 | 11.3±6.4     |
| gasping                       |              |     |    |     |      |     |     |    |     |              |
| yes                           | 122          | 3   | 0  | 0   | 1    | 2   | 0   | 0  | 0   | 2            |
| no                            | 231          | 8   | 7  | 3   | 13   | 6   | 6   | 4  | 8   | 26           |
| Pulmonary crackles at onset   |              |     |    |     |      |     |     |    |     |              |
| yes                           | 120          | 3   | 2  | 0   | 4    | 2   | 2   | 1  | 3   | 9            |
| no                            | 233          | 8   | 5  | 3   | 10   | 6   | 4   | 3  | 5   | 19           |
| Pleural effusion              |              |     |    |     |      |     |     |    |     |              |
| Yes                           | 15           | 2   | 1  | 0   | 1    | 0   | 0   | 0  | 1   | 1            |
| no                            | 340          | 9   | 6  | 3   | 13   | 8   | 6   | 4  | 7   | 23           |
| Extrapulmonary manifestations |              |     |    |     |      |     |     |    |     |              |
| yes                           | 102          | 0   | 0  | 1   | 2    | 1   | 0   | 0  | 1   | 3            |

17
| variables                  | M.pneumoniae | S.pneumoniae | X2   | p      |
|---------------------------|--------------|--------------|------|--------|
| N                         | 353          | 28           |      |        |
| gender                    |              |              |      |        |
| male                      | 246          | 20           | 2.06 | >0.05  |
| female                    | 107          | 8            |      |        |
| age                       | 7.8±4.1      | 7.9±3.5      | 0.13 | >0.05  |
| fever                     |              |              |      |        |
| yes                       | 302          | 21           |      |        |
| no                        | 51           | 7            | 1.5>0.05 |    |
| Duration of fever(days)   | 4.9±2.8      | 4.5±2.4      | 0.73 | >0.05  |
| Duration of cough(days)   | 10.2±6.2     | 11.3±6.4     | 0.90 | >0.05  |
| gasping                   |              |              |      |        |
| Yes                       | 122          | 2            |      |        |
| No                        | 231          | 26           | 8.88<0.01 |    |
| Pulmonary crackles at onset|              |              |      |        |

Table 5. Comparison between M.pneumoniae and S.pneumoniae with patients’ demographic and clinical characteristics
|                  | Yes | No | P-value |
|-----------------|-----|----|---------|
| Pleural effusion| 120 | 233| 0.05>0.05 |
| Extrapulmonary manifestations | 15 | 340 | 0.26>0.05 |
| WBC             | 245 | 251| 4.3<0.05 |
| ESR             | 36  | 317| 0.06>0.05 |
| CRP             | 81  | 272| 51.2<0.01 |
| Duration of hospitalization (days) | 15.8±4.1 | 15.3±4.4 | 0.62 | >0.05 |