Prevalence of Mycoplasma and Chlamydia Pneumonia in Severe Community-Acquired Pneumonia among Hospitalized Children in Thailand

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SUMMARY: Pneumonia is the leading cause of pediatric morbidity and mortality worldwide, and Mycoplasma pneumoniae and Chlamydia pneumoniae are the two most common atypical pathogens. This study was designed to determine the prevalence and clinical impact of mycoplasma and chlamydia pneumonia in children hospitalized with severe pneumonia. Children 1 month - 15 years old with a diagnosis of severe pneumonia (WHO criteria) were recruited between March 2005 and March 2006. Serologic studies were performed for anti-M. pneumoniae and anti-C. pneumoniae IgG/M on admission and 2-4 weeks afterward using ELISA. Of 52 patients, 13 (25%) were positive for Mycoplasma, 8 (15%) were positive for Chlamydia, 4 (7.6%) were positive for a mixed infection and 27 (52%) were negative. The subjects’ mean age was 23.8 ± 4.1 months. The mean of initial oxygen saturation on admission was 87.5 ± 1.2%. Fever and prolonged cough were the leading symptoms. The mean of hospitalization was 18.8 ± 2.6 days, chlamydia pneumonia had the longest duration, 30 ± 10.2 days and 13/52 (25%) study subjects developed respiratory failure. Only 10% were treated with adequate antibiotic prior to serologic results. There was one mortality (1/52, 2%). Our study suggests that mycoplasma and chlamydia infections are commonly found among children hospitalized with severe pneumonia. Coverage with an appropriate antibiotic should be considered to hasten recovery.

INTRODUCTION

Pneumonia is the most common cause of morbidity and mortality in young children worldwide (1-3), and the incidence is very high in developing countries (4). The term “atypical pneumonia” is used to describe pneumonia that is caused by atypical pathogens such as mycoplasma, or chlamydia or, less commonly, legionnaire infection. The clinical course among children infected with these pathogens is different from that of bacterial or viral infections. Most of them slowly progress and have no specific symptoms (5-8). The findings from chest x-ray are different from clinical presentations. Mycoplasma pneumoniae is the most common atypical pathogen found among children with community-acquired pneumonia (CAP), and Chlamydia pneumoniae (20%) is the second most common pathogen found after Mycoplasma. In Thailand, Limudomporn et al. previously reported infants (<6 months, n = 112) with lower respiratory tract infection who were infected with Chlamydia trachomatis (9). Principi and Esposito (10) studied children hospitalized for community-acquired lower respiratory tract infection (n = 613) due to M. pneumoniae and C. pneumoniae. M. pneumoniae was found in 34.3%, C. pneumoniae in 14.1% and co-infection in 6.8%. They classified patients into three disease groups: acute bronchitis, wheezing and pneumonia. In children with pneumonia, 60% had cough, 86% had fever and 85% had rales on chest examination. Only 15% had evidence of rhinitis. The mean duration of illness in these children was 13 days. Prapphal et al. (6) recently reported the prevalence and clinical presenta-

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MATERIALS AND METHODS

Study design: This study was a prospective analytic study to evaluate the prevalence of M. pneumoniae and C. pneumoniae infection in hospitalized children who were diagnosed with severe pneumonia that met established criteria.
Infants and young children 1 month to 15 years old with a diagnosis of severe pneumonia by inclusion criteria were recruited into the study. Written consent was obtained from their legal guardians or parents prior to the recruitment. This study protocol was approved by our institutional review boards (2005). In general, a patient was enrolled in the study if he or she met the following criteria (16): fever with body temperature (BT) >37.8°C, respiratory rate more than average per age by WHO criteria, abnormal chest x-ray together with signs of respiratory distress, e.g., use of respiratory accessory muscle with chest indrawing or measured with pulse oximetry demonstrated SpO2 <92% on room air. Patients were excluded if they were currently on macrolides antibiotics or were admitted to the hospital for more than 48 h. Upon enrollment, demographic characteristics and baseline clinical data were recorded. Pulmonary auscultation findings of each patient were recorded during detailed physical examination. Blood was drawn for initial anti-\(M.\ pneumoniae\) and anti-\(C. pneumoniae\) IgG or IgM. Venous blood samples were sent for hematologic and blood chemistry tests. Clinical course and treatment outcome were also recorded. Two to 4 weeks after enrollment, a second serum sample was obtained for assay of convalescent \(M. pneumoniae\) and \(C. pneumoniae\) antibody titers (gel particle agglutination). Patients were positive for \(C. pneumoniae\) if their serum IgM was positive (presence of IgM \(\geq 1/16\)). If serum IgM was negative (IgM \(\leq 1/16\)), then serum IgG was sent for IgG analysis (microimmunofluorescence [MIF]), and it was sent for for \(C. pneumoniae\) 2nd titer for paired serum (2-4 weeks later). The serological diagnosis was made if results were positive for anti-IgM titer \(\geq 1/16\) in either acute or convalescent serum, or if results showed very high titers of IgG antibody \(\geq 1/512\) or a 4-fold or greater titer change between sera. IgG titers ranging from 16 to 256 were considered negative.

**Statistical analysis:** SPSS software (version 13, 2005) was used for statistical analysis. Descriptive data was presented as the mean ± SE. Categorical data were analyzed with the chi-square test or Fisher’s exact test. Multiple comparison (ANOVA) was used to compare the mean in different groups with post hoc analysis. For all of the statistical analysis, \(P < 0.05\) was considered statistically significant.

### Table 1. Summary of the baseline clinical data of children enrolled in the study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Infants infected with M. pneumoniae (Mean ± SE)</th>
<th>Infants infected with C. pneumoniae (Mean ± SE)</th>
<th>Both (Mean ± SE)</th>
<th>Unidentified (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (month) Mean ± SE</td>
<td>21.3 ± 7</td>
<td>49.1 ± 19.3</td>
<td>23.7 ± 5.5</td>
<td>17.5 ± 3.6</td>
</tr>
<tr>
<td>*Duration (day) of Fever</td>
<td>5.2 ± 1</td>
<td>5.5 ± 1.9</td>
<td>2.3 ± 0.9</td>
<td>5.7 ± 0.98</td>
</tr>
<tr>
<td>Cough</td>
<td>5.3 ± 1</td>
<td>8.1 ± 2.3</td>
<td>1.5 ± 0.3</td>
<td>5.8 ± 0.9</td>
</tr>
<tr>
<td>Body temp (°C)</td>
<td>38 ± 0.3</td>
<td>37.7 ± 0.5</td>
<td>38.1 ± 0.7</td>
<td>37.9 ± 0.15</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>2 ± 0.5</td>
<td>5 ± 1.7</td>
<td>1.3 ± 0.2</td>
<td>2.9 ± 0.6</td>
</tr>
<tr>
<td>Physical exam</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rales (%)</td>
<td>53.8</td>
<td>75</td>
<td>100</td>
<td>85</td>
</tr>
<tr>
<td>Wheezing (%)</td>
<td>38</td>
<td>12.5</td>
<td>25</td>
<td>29.6</td>
</tr>
<tr>
<td>Rhonchi (%)</td>
<td>23</td>
<td>50</td>
<td>25</td>
<td>40.7</td>
</tr>
<tr>
<td>Oxygen saturation (initial) (%)</td>
<td>88.5 ± 2.2</td>
<td>88.9 ± 2.4</td>
<td>91.3 ± 1.3</td>
<td>86.2 ± 1.8</td>
</tr>
<tr>
<td>Co-morbidity (%)</td>
<td>38</td>
<td>87.5</td>
<td>75</td>
<td>51.8</td>
</tr>
<tr>
<td>Duration (day) of hospitalization</td>
<td>8</td>
<td>20</td>
<td>11.5</td>
<td>13</td>
</tr>
</tbody>
</table>

*a Symptoms prior to hospitalization.*
Among them, 3 had *M. pneumoniae* and 2 had *C. pneumoniae* infection. The average length of hospitalization was at 18.8 ± 2.6 days. The longest hospital stays were found in children with *C. pneumoniae* infection (n = 8; 30 ± 10.2 days) (Fig. 2). Additionally, one patient with *C. pneumoniae* infection eventually expired.

**DISCUSSION**

Atypical pathogens are one of the most important causes of pneumonia in children at all ages. Specifically, CAP in young children often requires ICU admission, as these pneumonia patients have the highest mortality rate (1,15). Previous studies indicated a high incidence of infections in children with CAP (6 - 40%); this may play a considerable role in any closed community (10). A recent study in Southeast Asia on the prevalence of atypical respiratory pathogens in CAP found *M. pneumoniae* in 12.2% and *C. pneumoniae* in 4.7% (n = 1,756) of CAP patients. Further, a subgroup analysis in Thai children reported by Prapphal et al. (6) showed that *M. pneumoniae* was found in 14% and *C. pneumoniae* in only 3.4% (n = 292). Lobar consolidation was the common feature among children infected with atypical pathogens. They were less likely to have dyspnea at presentation. Compared to our study, which looked into a specific group of children with severe CAP, we found that almost half of these children (25/52, 48%) were positive either for *M. pneumoniae* or *C. pneumoniae*. Thus, the clinical presentations of atypical pneumonia could indeed vary from asymptomatic to severe, as shown in our cases. Moreover, this confirmed the potentially significant impact from atypical pathogens in severe CAP that we usually ignored the importance. Our data also demonstrated that children who were infected with *C. pneumoniae* had the longest hospitalization, with one mortality. This may be explained by their underlying illness (7/8, 87.5%).

Roles of *M. pneumoniae* and *C. pneumoniae* infection in hospitalized children (n = 613) were previously reported by Principi and Esposito (10), who found that almost half of their patients were positive for *M. pneumoniae* and/or *C. pneumoniae*. Their prevalence was in agreement with our data. *M. pneumoniae* and *C. pneumoniae* co-infection was also found in our study, but its clinical implications were not clear. This kind of infection has been increasingly recognized over the years (10,17), and identification of the complex etiology of lower respiratory tract infections is indeed an important step toward providing effective treatment. A report by Prapphal...
et al. found that chest x-ray showing lobar infiltration at presentation might predict atypical infection. Most of our children infected with these atypical pathogens tended to have patchy or lobar infiltrations. However, we could not find that the incidence was statistically significant. Of our patients who were positive for *M. pneumoniae* and *C. pneumoniae*, 38 and 12.5% presented with wheezing, respectively. Encephalopathy was found in 3 of the patients with mycoplasma pneumonia, in 2 of the patients with chlamydia pneumonia infection and therein 3 patients from the unidentified group. Additionally, a few previous studies emphasized the role of atypical pathogens in severe CAP, especially in children admitted to PICU (18,19). Thirteen (25%) patients developed respiratory failure and were transferred to PICU. Five of them (38%) were positive for atypical pathogens (*M. pneumoniae*, 2, *C. pneumoniae*). In our study, there were only 5 (20%) patients who were given appropriate antibiotics prior to hospitalization (that is, a spectrum drug with coverage for atypical pathogens). If antibiotic treatment had been started earlier, it would have helped to reduce the number of recurrent respiratory episodes, decreased morbidity rates and shortened the duration of symptoms. Thus, physicians should consider using empirical antibiotics that have a wide spectrum coverage that includes these organisms to treat severe cases while waiting for the results of serologic study (20).

Studies in the past (10) showed that the most common findings of atypical pneumonia were fever (92%), leukocyte count above 10,000/mm³ (56%) and bilateral infiltrations (60%) (10). We also found that children infected with *M. pneumoniae* tended to have leukocytosis (10/12, leukocyte > 10,000/mm³). In contrast to other studies, we found that children infected with *C. pneumoniae* tended to have lower leukocyte (OR = 2.48 [1.3 - 4.5]; *P* < 0.05). One limitation of this study was the absence of testing for respiratory viruses because of our small budget. Thus, it is possible that respiratory viruses also could act as cofactors in rendering subjects more susceptible to other stimuli such as these atypical pathogens.

In conclusion, our results emphasized the role of *M. pneumoniae* and *C. pneumoniae* in children with severe CAP (even in children less than 3 years old). These atypical bacterial infections could lead to greater morbidity and mortality in susceptible individuals when they are not adequately treated.

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