

Prevalence and Clinical Features of Mycoplasma Pneumoniae in Thai Children

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Objective: To determine the prevalence and clinical features of mycoplasma pneumoniae in Thai children with community acquired pneumonia (CAP).

Material and Method: Diagnosis of current infection was based on ≥ 4 fold rise in antibody sera or persistently high antibody titers together with the presence of mycoplasma DNA in respiratory secretion. The clinical features were compared between children who tested positive for *M. pneumoniae*, and those whose results were negative.

Results: Current infection due to *M. pneumoniae* was diagnosed in 36 (15%) of 245 children with paired sera. The sensitivity and specificity of polymerase chain reaction (PCR) in diagnosing current infection in the present study were 78% and 98% respectively. The mean age of children with mycoplasma pneumoniae was higher than CAP with unspecified etiology. The presenting manifestations and initial laboratory finding were insufficient to predict mycoplasma pneumoniae precisely, the presence of chest pain and lobar consolidation on chest X-ray, however, were significant findings in children with mycoplasma pneumoniae.

Conclusion: The present study confirms that *M. pneumoniae* plays a significant role in CAP in children of all ages. Children with this infection should be identified in order to administer the appropriate antibiotic treatment.

Keywords: Prevalence, Mycoplasma pneumoniae, Children, Clinical

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M. pneumoniae is one of the most common causes of community-acquired pneumonia (CAP) in children and adults⁽¹⁾. This organism is reported to be the most frequent 'atypical' pathogen responsible for CAP^(1,2). The prevalence of *M. pneumoniae* varies greatly from study to study depending on the population and diagnostic methods⁽³⁻⁷⁾. In Thailand, studies to determine prevalence and clinical features of *M. pneumoniae* have been carried out⁽⁸⁻¹²⁾. Most of them,

however, are serological studies and most are studies in adult patients. Serological testing has some limitations because a convalescent serum specimen is required⁽¹³⁾. Polymerase chain reaction (PCR) has recently been found to be useful for rapidly detecting this pathogen in respiratory secretion, however, the cost is expensive and it is not available in most health care settings^(14,15). Therefore, good epidemiological data on the prevalence and clinical features of CAP due to *M. pneumoniae* in Thai children is still lacking. The aim of the present study was to evaluate the prevalence and clinical features of mycoplasma pneumonia in Thai children, following the introduction of standardized diagnostic tests for detection of *M. pneumoniae*.

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Material and Method

Study design

This prospective multi-centered study was conducted from December 2001 to November 2002 at three hospitals in Bangkok: Queen Sirikit National Institute of Health; King Chulalongkorn Memorial Hospital; and Ramathibodi Hospital. The study design was approved by the Research Review Board and Ethics Committee of each hospital. Written informed consent was obtained from all patient's legal representatives before the study enrollment.

Patients

Children aged 2-15 years with clinical and radiological diagnosis of CAP were considered eligible for inclusion. CAP was defined as: new infiltrates or consolidation on chest X-ray that could not be attributed to other etiology; and the presence of 3 or more of the following signs and symptoms: cough, acute change in the quality of sputum, fever or hypothermia ($> 38^{\circ}\text{C}$ or $< 36.1^{\circ}\text{C}$) within the preceding 24 hours, rales or evidence of pulmonary consolidation, leukocytosis, malaise / myalgia or gastrointestinal symptoms. Children were excluded if they had evidence or history of tuberculosis, nosocomial pneumonia, aspiration pneumonia, and bronchiectasis. Those who were HIV-positive or who had been hospitalized within 2 weeks prior to consultation were also excluded.

Laboratory tests

All laboratory tests were done at the Clinical Immunology Laboratory, Department of Pathology, Faculty of Medicine, Ramathibodi Hospital. To ensure that all centers used the standardized protocol for specimen collection, a training workshop was carried out before the start of the present study. A courier service was hired to transport the specimens when they were ready for collection. An External Quality Assurance System program was carried out twice during the study to assess the competency of laboratory in PCR assays. Acute and convalescent (2-4 weeks apart) sera were collected aseptically for serologic testing. Throat swabs, sputum, or nasopharyngeal aspirate, were collected for PCR analysis.

Specific antibodies to *M. pneumoniae* were measured using a particle agglutination test (Serodia Myco II, Fujirebrijo, Japan). PCR assays for the detection of *M. pneumoniae* nucleic acids were performed with primers targeting the p1 adhesin gene of *M. pneumoniae*⁽¹⁶⁾. The presence of a PCR product of 209 bp size on gel electrophoresis was considered indica-

tive of infection with *M. pneumoniae*.

Criteria for etiologic diagnosis

Current infection with *M. pneumoniae* was based on 4-fold or greater rise in antibody titers between paired acute and convalescent sera. Results of single serum samples were excluded from the analysis. In cases with high antibody titers (IgG) in both serum samples ($\geq 1:160$), the presence of positive PCR for *M. pneumoniae* in respiratory secretions was also considered as current infection. The presence of positive PCR for *M. pneumoniae* in the absence of a positive serologic response was interpreted as possible carriage.

Data analysis

Chi-square or Fisher's exact test was used to determine the significant difference in proportions between groups. Student's t-tests were used to compare continuous variables. A *p*-value of less than 0.05 was considered to indicate statistical significance.

Results

Patient characteristics

Of the 257 enrolled children with a diagnosis of CAP, paired sera could be obtained from 245 children and provided the basis for estimating the rate of infection caused by *M. pneumoniae*. Of these children, 135 (55%) were male. The mean age of the children was 4.7 ± 3.0 years; 166 patients (68%) were under 5 years old, 51 (21%) were 5-9 years old and 28 (11%) were 10-15 years old. In total, 199 (81%) were treated in the hospitals and three children (1%) required treatment in the intensive care unit. One hundred and eighty-nine children (77%) had previous antibiotic therapy. Many children had co-morbidities: 51 (21%) had asthma, seven (3%) had congestive heart failure, one child had hepatic disease, and one child had renal impairment. CAP due to *M. pneumoniae* occurred throughout the study period. No definite seasonal preference was noted (Fig. 1).

Etiologic diagnosis

Thirty-six (15%) of the 245 children met the diagnostic criteria for *current M. pneumoniae* infection. Twenty-four children (10%) were diagnosed by a 4-fold or greater increase in antibody titer between acute- and convalescent-phase sera. Twelve (5%) were diagnosed by positive PCR with persistent high antibody titer. Sixteen (67%) of the seroconversion cases were also positive by PCR and eight (33%) were PCR

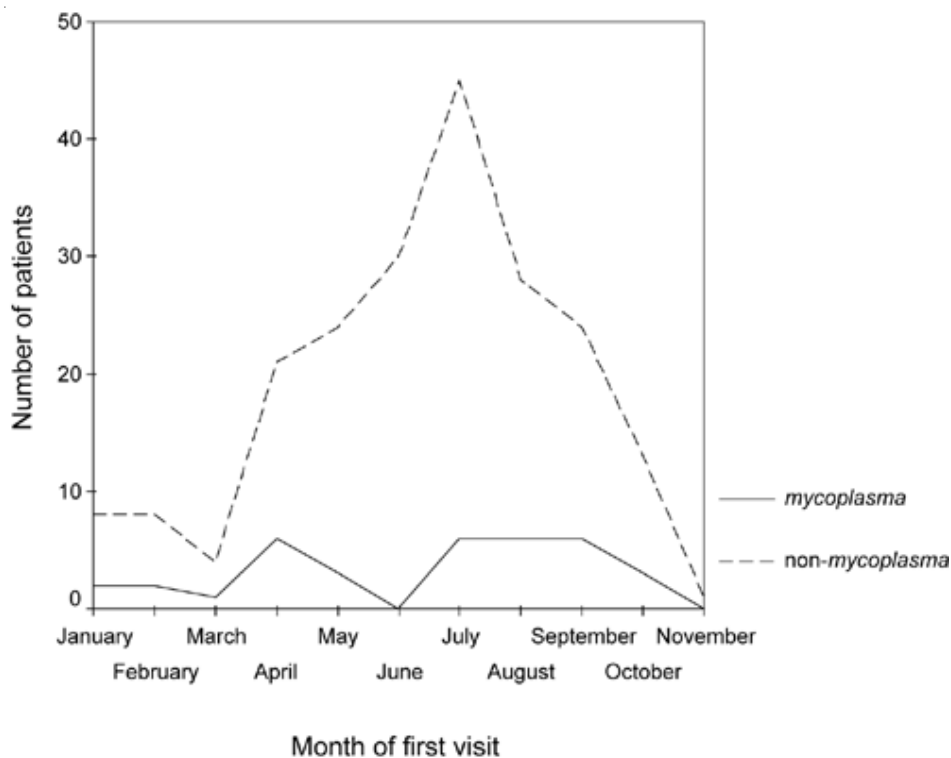


Fig. 1 Monthly distribution of mycoplasma pneumoniae and other CAP

negative. When using PCR result alone, the infection rate decreased to 14% (34/245 cases). Six children had positive PCR of *M. pneumoniae* without serological evidence of acute infection and were considered as possible carriage.

Comparison between mycoplasma pneumonia and unspecified pneumonia

The clinical characteristics of the study population at enrolment are summarized and compared between CAP caused by *M. pneumoniae* and other unspecified etiology (Table 1). The mean age of children with mycoplasma pneumonia was significantly higher than CAP with non-mycoplasma pneumonia (6.3 ± 3.5 vs 4.5 ± 2.9 , $p = 0.001$). The prevalence of mycoplasma pneumonia increased with age (Fig. 2). Coughing and fever were the most common presenting symptoms in both groups of CAP. The most common findings on physical examination were rales. There was no significant difference in symptoms and signs between mycoplasma pneumonia and non-mycoplasma pneumonia, except for the presence of chest pain, which is more common in mycoplasma pneumonia than other

childhood pneumonia (19.4% vs 6.7%, $p = 0.04$). Asthma was the most common co-morbidity in both groups of CAP.

For laboratory data, no significant difference was detected in total and differential WBC count between children with mycoplasma pneumonia and non-mycoplasma pneumonia. The radiographic characteristics of the study population are shown in Table 2. The most common radiographic findings in both groups of children were patchy infiltration and interstitial infiltration. In the present study, lobar consolidation was the only chest X-ray finding that was significantly higher in children with mycoplasma pneumonia than those with unspecified pneumonia (11.1% vs 1.9%, $p = 0.02$).

Discussion

M. pneumoniae is one of the common causes of CAP in children. The reported prevalence of *M. pneumoniae* in Thailand varied from 6-40%⁽⁸⁻¹²⁾. This wide variation may be due to the age difference of the patients in the studied group and the diagnostic criteria.

Table 1. Comparison of *mycoplasma pneumoniae* and non-*mycoplasma pneumoniae*

Characteristics	<i>Mycoplasma pneumoniae</i> (n = 36) (%)	Non- <i>mycoplasma pneumoniae</i> (n = 209) (%)	p-value
Male : Female	24:12	111:98	NS
Mean age (years) (X±SD)	6.3±3.5	4.5 ± 2.9	0.001
ICU admission	0	3 (1.5)	NS
Symptoms & signs:			
- Cough	36 (100)	209 (100)	NS
- Fever	34 (94.4)	205 (98.1)	NS
- Chill	8 (22.2)	36 (17.2)	NS
- Chest pain	7 (19.4)	14 (6.7)	0.04
- Dyspnea	24 (66.7)	164 (78.5)	NS
- Malaise	16 (44.4)	97 (46.4)	NS
- Myalgia	5 (13.9)	27 (12.9)	NS
- Diarrhea	5 (13.9)	31 (14.8)	NS
- Wheezing	6 (16.7)	49 (23.4)	NS
- Rales	33 (91.7)	188 (90.0)	NS
- Rhonchi	14 (38.9)	103 (49.3)	NS
- Bronchial breath sound	1 (2.8)	9 (4.3)	NS
Co-morbidity:			
- Asthma	8 (22.2)	43 (20.6)	NS
- Hepatic disease	0	1 (0.5)	NS
- Impaired renal function	1 (2.8)	0	NS
Previous antibiotics	29 (80.6)	160 (76.6)	NS

NS = Not statistical significance

Table 2. Chest roentgenographic findings in patients with *mycoplasma pneumoniae*

Findings	<i>Mycoplasma pneumoniae</i> (n = 36)	Non- <i>mycoplasma pneumoniae</i> (n = 209)	p-value
Consolidation (%)	4(11.1)	4 (1.9)	0.018
Patchy (%)	19 (52.8)	98 (46.9)	NS
Interstitial (%)	14 (38.9)	114 (54.5)	NS
Perihilar (%)	0	4 (1.9)	NS
Atelectasis (%)	1 (3.8)	3 (1.4)	NS
Effusion (%)	1 (3.8)	3 (1.4)	NS

The present study is a large, prospective, multicenter study of pediatric CAP in Bangkok during a one-year study period. The infection rate of *M. pneumoniae* in the present study is 15%, comparable to that reported by Michelow et al⁽¹⁷⁾, and Esposito et al⁽¹⁸⁾, despite the fact that our study was conducted in a different location and different time.

In the past, culture was used as a reference to evaluate new diagnostic test. However, culturing *M. pneumoniae* from clinical specimens is laborious and

may take up to 5 weeks⁽¹⁹⁾. Moreover, the sensitivity of culture is lower than that of serological assays⁽²⁰⁾. Serological testing is the most common means of diagnosing *M. pneumoniae* in routine clinical practice, but it often only provides a retrospective diagnosis of acute infection because a convalescent serum specimen is needed to show seroconversion. It is therefore not optimum for patient management^(15,21). Recently, PCR has become an optional method for the rapid detection of *M. pneumoniae* in a clinical specimen^(21,22). The

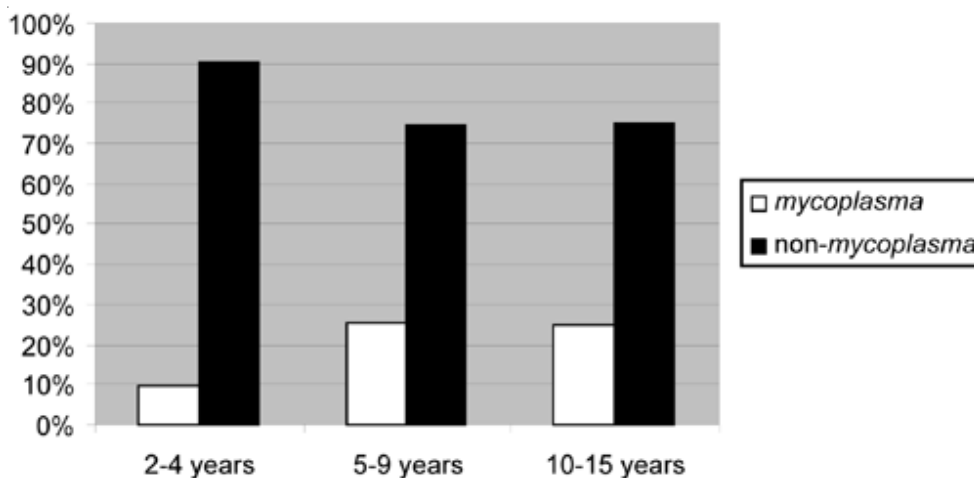


Fig. 2 Age distribution in children with *mycoplasma pneumoniae*

advantages of PCR techniques over culture and serology are that they allow the identification of pathogens in specimens that have not been properly handled or frozen. They also have the advantage that a diagnosis can be made after testing a single specimen⁽¹⁵⁾ but it carries the risk of detecting healthy carriers of *M. pneumoniae*⁽¹⁹⁾. In the present study, the authors combined both serology and PCR finding for diagnostic criteria. PCR was positive in 28 of 36 children who were diagnosed as current *M. pneumoniae* infection. Thus, the sensitivity of the PCR in diagnosing acute *M. pneumoniae* infection in the present study was 78%. PCR was also positive in 6 of 209 children who had no serological evidence of infection and was considered as false positive from possible carriage. Therefore, the specificity of PCR in the present study was 97%.

In the present study, PCR finding could identify 12 children with *M. pneumoniae* infection who had no seroconversion. However, if PCR had been used as the single test, diagnosis would not have been established in eight children. This finding confirms the suggestion that PCR should be used for rapid diagnosis of *M. pneumoniae* infection. In case of a negative PCR, serological test on paired sera is necessary to either confirm or reject the diagnosis⁽¹⁹⁾.

In the present study, the authors found an age-dependent increase in the occurrence of *M. pneumoniae* infection in children with CAP as has been observed in previous report^(23,24). Moreover, as others have observed elsewhere^(17,23-25), the authors found that the prevalence of mycoplasma pneumonia in children

younger than 5 years old was not uncommon (44% of mycoplasma pneumonia group).

Concerning clinical presentations, many studies have shown that it is not possible to predict mycoplasma pneumonia on the basis of presenting manifestations^(15,23,26). The results of the present study are similar to previous reports. The authors found no clinical difference between CAP caused by *M. pneumoniae* and CAP of unspecified etiology except for the presence of chest pain that is likely to indicate mycoplasma pneumonia. Chest pain has been reported to be the common finding in adults with mycoplasma pneumonia up to 40-60%^(11,22).

Similar to previous reports^(18,23,26), white blood cell and differential counts could not differentiate the etiologic agents of CAP in the presented population. On the chest radiograph, the authors found that lobar consolidation was more common in children with mycoplasma pneumonia than children with non-mycoplasma pneumonia. This finding has been reported in a study of children admitted to hospital with pneumonia by Clements et al⁽²⁷⁾.

Conclusion

M. pneumoniae is a common cause of CAP in Thai children. The prevalence of 15% in the present study is similar to that observed in Western countries. The combination of a serological test and PCR increase the sensitivity in diagnosing this infection. Chest pain and lobar consolidation were significantly associated with mycoplasma pneumonia in the present study. The present study confirms the significance of mycoplasma

pneumonia in children of all age groups and should be taken into account when starting antibiotics for children with CAP.

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ความชุกและลักษณะทางคลินิกของโรคปอดบวมจากเชื้อมัคโคพลาสมาในผู้ป่วยเด็กไทย

จิตลัดดา ดีโรจนวงศ์, นवलจันทร์ ปราบพาล, สุภรี สุวรรณจุฑะ, สรศักดิ์ โฉมจินดารัตน์, ธีรชัย ฉันทโรจนศิริ, มงคล คุณากร, ธีญญณัฐ บุนนาค, พนิดา ศรีสันต์

วัตถุประสงค์: ศึกษาความชุกและลักษณะทางคลินิกของการติดเชื้อ *M.pneumoniae* ในผู้ป่วยเด็กโรคปอดบวม
วัสดุและวิธีการ: ตรวจระดับแอนติบอดีในซีรัม และตรวจ DNA ของ *M. pneumoniae* ในสารคัดหลั่งจากทางเดินหายใจระดับแอนติบอดีเพิ่มเป็น 4 เท่า หรือ ระดับสูงต่อเนื่องร่วมกับตรวจพบ DNA จะวินิจฉัยว่าติดเชื้อ *M. pneumoniae* เปรียบเทียบลักษณะทางคลินิกของกลุ่มนี้กับกลุ่มที่ให้ผลลบ

ผลการศึกษา: การติดเชื้อ *M. pneumoniae* พบได้ 36 รายจากผู้ป่วย 245 ราย (ร้อยละ 15) ความไวและความจำเพาะในการวินิจฉัยการติดเชื้อ *M. pneumoniae* โดยวิธี PCR ในการศึกษาเป็นร้อยละ 78 และ 98 ตามลำดับ อายุเฉลี่ยของเด็กที่ติดเชื้อ *M. pneumoniae* สูงกว่าปอดบวมจากสาเหตุอื่นอย่างมีนัยสำคัญทางสถิติ และพบว่าอาการเจ็บหน้าอกและ lobar consolidation ในภาพรังสีปอดสัมพันธ์กับการติดเชื้อ *M. pneumoniae* อย่างมีนัยสำคัญทางสถิติ

สรุป: การศึกษานี้ยืนยันว่า *M. pneumoniae* เป็นสาเหตุสำคัญของปอดบวมในเด็กทุกอายุ การวินิจฉัยที่ถูกต้องจะช่วยในการเลือกใช้ยาปฏิชีวนะที่เหมาะสม