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Epidemiology and clinical profiles of *Mycoplasma pneumoniae* infection in hospitalized infants younger than one year

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Summary
Background: *Mycoplasma pneumoniae* (*M. pneumoniae*) is an important pathogen of community-acquired pneumonia in children, but the epidemiology and clinical features of *M. pneumoniae* infection in infants are reported in only a few studies. This study aims to evaluate possible age-related differences in the presenting clinical features in infants with *M. pneumoniae* infection.
Methods: 24-month longitudinal study on lower respiratory tract infection (LRTI) caused by *M. pneumoniae*, confirmed by both serology and polymerase chain reaction, was performed. Medical records of patients were reviewed for demographic, clinical and microbiological characteristics.
Results: Out of 2174 infants with LRTI admitted to the Children's Hospital Affiliated to Soochow University in Jiangsu Province, 80 were diagnosed with *M. pneumoniae* infection. We found that 15 were aged 1 to <5 months; 29 were aged 5 to <9 months; and 36 were aged 9 to <12 months. *M. pneumoniae* infection mainly occurred in August to October. The presence of fever with a maximum temperature of >39.0 °C for ≥3 days was more common in the 9 to <12 month age group ($P < 0.05$). Laboratory tests showed that the infants aged 9–12 months had a higher peripheral leukocyte ($P = 0.035$) and neutrophil ($P = 0.015$) count and a higher CRP level ($P = 0.041$). Moreover, the median length of hospitalization for infants aged 1 to <5 months was shorter than that in the other two groups.

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Conclusion: Our work provides important clinical information about infants with *M. pneumoniae* infection and highlights that younger infants with *M. pneumoniae* infection may have a milder clinical course than older infants.

M. pneumoniae (*M. pneumoniae*) causes upper and lower respiratory tract infections in all age groups [1]. However, it is one of the most important etiologic agents that causes community-acquired pneumonia in children, and accounts for 10—40% of community-acquired pneumonia cases [2—5].

M. pneumoniae does not have the ability to synthesize peptidoglycan cell walls, and it has innate resistance against all beta-lactams and glycopeptide antibiotics [1]. Therefore, correct and rapid diagnosis of *M. pneumoniae* infections is critical for initiating appropriate antibiotic treatment. *M. pneumoniae* pneumonia (MPP) presents with several manifestations, such as fever, cough, wheezing, diarrhea, vomiting and other non-specific symptoms [6,7]. However, it is impossible to diagnose MPP merely based on these signs and symptoms, and laboratory analysis is more important for detecting *M. pneumoniae* infection [8,9]. In our department, polymerase chain reaction (PCR) technology and serological assays are the common laboratory diagnostic methods used to detect *M. pneumoniae* infection.

Community-acquired *M. pneumoniae* epidemics typically present in school-aged children and young adults [3,4,10,11]. However, an increasing number of studies indicate that *M. pneumoniae* infection is frequent in children aged 1—5 years, and that the clinical features differ between younger and older patients [12,13]. *M. pneumoniae* infection in young children has been receiving more and more attention [14]. Due to the limited amount of data on *M. pneumoniae* infection in infants younger than 1 year in the literature, we performed a two-year longitudinal retrospective study to describe the epidemiology and the clinical features of lower respiratory tract infection (LRTI) caused by *M. pneumoniae* in infants admitted to a tertiary children's hospital, and aimed to evaluate possible age-related differences in the presenting clinical features.

Patients and methods

Patients

This retrospective descriptive study was conducted over a 24-month period (January 1, 2012 to December 31, 2013) on children aged 1 month to 12 months and presenting with LRTIs (n = 2174) at the Children's Hospital Affiliated to Soochow University, China. Children were eligible for enrollment based on the presence of the following symptoms: (a) Fever, cough and dyspnea (clinical findings); and abnormal breath sounds, wheezes or crackles (ausculatory findings); and/or focal/segmental consolidation, interstitial changes or pleural effusion (radiological findings) that confirmed LRTI. (b) Both positive PCR and positive IgM findings at admission or at follow-up, or a $\geq$4-fold rise in the IgG titer.

Children were excluded if they had been born prematurely or had severe concomitant diseases such as neoplasms, kidney or liver dysfunction, immunosuppression, chronic disorders of the pulmonary or cardiovascular system, genetic or neurological disorders and chronic metabolic diseases.

The study was approved by the Ethics Committee of Soochow University, and written informed consent was obtained from the parents.

Data collection

Medical records were reviewed for the following: (1) *M. pneumoniae* diagnostic tests performed using both nasopharyngeal swabs and serum samples; (2) clinical data, such as gender, age, year and month of hospitalization, antibiotic therapy during the preceding 2 weeks, exclusive breastfeeding during the first 4 months of life, duration of symptoms before admission, previous hospitalization, history of wheezing, length of fever, maximum temperature, cough, fever, wheezing and gastrointestinal symptoms (diarrhea or vomiting); (3) disease severity parameters including length of hospitalization, requirement for supplemental oxygen, and admission to the PICU [15,16]; (4) laboratory data, such as peripheral leukocyte, neutrophil and lymphocyte counts, C-reactive protein (CRP) levels and chest radiography findings; and (5) the results of the direct fluorescent antibody test for seven common viruses (respiratory syncytial virus; adenovirus; influenza virus A and B; and parainfluenza virus 1, 2 and 3), real-time PCR for human Bocavirus (hBov), and reverse-transcription PCR for human metapneumovirus (hMPV) with nasopharyngeal swab samples.

Real-time PCR

Samples for PCR testing were obtained from the nasopharynx within 24 h of admission. A quantitative diagnostic kit (DaAn Gene Co. Ltd., Guangzhou, China) was used to analyze *M. pneumoniae* DNA, as previously reported [17]. The method is based on the TaqMan PCR method, and the target is 16S rRNA genes specific for the *M. pneumoniae* genome. Briefly, 1 mL of nasopharyngeal aspirate (NPA) diluted with 4% NaOH was centrifuged at 12,000 rpm for 5 min. The sediment was collected, washed twice with 0.9% NaCl, blended with 50 μL of DNA extraction solution, incubated at 100 °C for 10 min, and centrifuged at 12,000 rpm for 5 min. Real-time PCR was performed on the resulting supernatant (2 μL) and PCR mix (43 μL) (supplied with the kits) using the Applied Biosystem 7500 real-time