

Original article

Mycoplasma infection in Malaysian children: laboratory investigation and antimicrobial therapy

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Abstract:

Background: *Mycoplasma pneumoniae* (*M. pneumoniae*) is an important causative agent of childhood infection with variable clinical presentations. The objective of the study was to evaluate the laboratory investigation and antimicrobial therapy of *M. pneumoniae* infection in children admitted to paediatric ward. **Materials & Methods:** A total of 111 children, of which 59 (53.2%) boys and 52 (46.8%) girls, with median age of 2 years (inter quartile range 1-6 years) with suspected *M. pneumoniae* infection were tested for IgM by enzyme-linked immunosorbent assay (ELISA). The children were classified as seropositive and seronegative. **Results:** Of the 111 children, 45 (40.5%) had serological evidence of *M. pneumoniae* infection and the remaining 66 (59.5%) were seronegative. There was significant association ($p < 0.001$) between age and serology response. Seropositive children were more likely to be older (median age 5.0 [interquartile range 2- 7] years, $p < 0.001$). Children with *M. pneumoniae* infection were less likely to have cough ($p = 0.023$) in which 55 (65.5%) patients having cough were seronegative. There was no significant association between laboratory findings of full blood count and serology. **Conclusion:** In addition to clinical and laboratory features, other factors like age group and absence of cough might be helpful in predicting *M. pneumoniae* infection.

Key words: children; *Mycoplasma pneumoniae*; enzyme linked immunosorbent assay; pneumonia; atypical pneumonia; antimicrobial therapy

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Introduction

Mycoplasma is the smallest and simplest self limiting bacteria. It is the commonest cause of primary atypical pneumonia resistant to β -lactam antibiotics in older children and young adults. Clinical diagnosis of *Mycoplasma pneumoniae* pneumonia is difficult as viral and other pneumonias show similar clinical features. Numerous studies were undertaken that provided new insights into the various clinical pre-

sentations associated with *M. pneumoniae* infection.^{1,2} Few reports showed that it could also cause severe disease not limited to the respiratory tract but involving extra-pulmonary manifestations.³ The most common clinical findings of these patients were cough and fever where most of them had benign course and survived. The white blood cell count was often normal. However, extensive pneu-

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monia can produce a profound leukocytosis.¹ In a clinical setting where *M. pneumoniae* infection is suspected, serology is often used in diagnosis.

Previous studies compared the clinical features of patients with *M. pneumoniae* pneumonia to other pathogens and these studies were predominantly adult case series rather than involving children.² A study done in Singapore and Finland showed that the majority of *M. pneumoniae* infections were in school-aged children.⁴ The increasing seroprevalence rates of *M. pneumoniae* after 2 years of age should alert clinicians to consider the organism in the differential diagnosis of infectious diseases in this age group.⁵

Hence, the above prompted us to conduct a study on clinical features, laboratory investigation and antimicrobial therapy of children infected with *M. pneumoniae* in the paediatric ward of our tertiary hospital, Universiti Kebangsaan Malaysia Medical Centre.

Materials & methods

Study population: A retrospective cross-sectional study was conducted on 111 paediatric patients at Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from January 2010 to December 2012. Patients who admitted to the paediatric ward and suspected to *M. pneumoniae* infection were included in the study. However, the patients those had underlying lung disease, obtained insufficient sera samples were excluded from the study.

Demographics: The patients' list was obtained from Medical Microbiology Department and the medical records were traced via the record office of UKMMC. They were categorised into two distinct groups based on the results of serological tests.

Clinical manifestations': Clinical information was obtained tracing the medical report of record file of UKMMC. All the manifestations were tabulated from the patients under study.

Diagnostic test: Enzyme-linked immunosorbent assay (ELISA) was used to detect IgM antibody of the suspected children of *M. pneumoniae* infection. The test was performed as per the manu-

facturer's recommendation (*Mycoplasma pneumoniae* IgM-ELISA Kit , Nova Tec Immunodiagnostica GmbH, Waldstr.23 A6 D-63128 Dietzenbach, Germany). The children were classified as seropositive and seronegative based on the results.

Statistical analysis: Results were analysed using IBM SPSS Statistics 21. *P* < 0.05 was considered to be statistically significant.

Results:

Demographics: A total of 111 children admitted during the study period were analysed. Forty-five (40.5%) children had serological evidence of *M. pneumoniae* infection. Children with positive *M. pneumoniae* serology were more likely to be older (median age 5.0 [interquartile range 2- 7] years, *p* < 0.001).

Clinical manifestations: The predominant symptoms were fever and cough which occurred in 99 (89.2%) and 84 patients (75.7%) respectively. Among those having fever, 49 (44.1%) had fever for more than six days. Table 1 compares the clinical parameters between the two groups. There was significant association between cough and serology response whereby patients with cough were more likely to be seronegative (55, 65.5%; *p* = 0.023). There was no association found with other clinical manifestations.

Crackles were the commonest physical sign where 49 (44.1%) patients had crackles during auscultation. Tachypnoea was recorded in 47 patients (42.3%) and bronchial breathing in 9 (8.1%) patients.

Table : 1: Clinical features of Mycoplasma pneumonia suspected children

	Seropositive	Seronegative	<i>p</i> -value
Family members with cough	8 (32%)	17 (68%)	0.323
Fever > 6 days	19 (38.8%)	30 (61.2%)	0.736
Fever	40 (40.4%)	59 (59.6%)	1.000
Cough	29 (34.5%)	55 (65.5%)	0.023
Rhinnorrhoea	21 (35.6%)	38 (64.4%)	0.258
Wheeze	6 (35.3%)	11 (64.7%)	0.632
Headache	4 (66.7%)	2 (33.3%)	0.361
Breathlessness	7 (33.3%)	14 (66.7%)	0.455
Lethargy	16 (45.7%)	19 (54.3%)	0.451
Tachypnoea	16 (34%)	31 (66%)	0.232
Crackle	18 (36.7%)	31 (63.3%)	0.468
Bronchial Breath	3 (33.3%)	6 (66.7%)	0.916

€ Chi Squared Test

Laboratory evaluation: In general, total white cell count (median [interquartile range] :11.7 [6.6 –

15.9] $10^9/L$) (Table -11) increased for the patients and it was slightly higher lymphocyte count (3.2 [1.8 – 5.1] $10^9/L$). The other parameters, such as haemoglobin (11.8 [10.6 – 12.4] $10^9/L$), neutrophil (6 [3.2 – 9/8] $10^9/L$) and platelet (311 [220 – 425] $10^9/L$), were in the normal range. When comparing between the two groups, there were no significant difference in the full blood count parameters.

Table: 2: Full blood count parameters on admission in the study population

	Seropositive (median (IQR))	Seronegative (median (IQR))	p- value □
Hemoglobin (g/dL)	12.0 (1.7)	11.5 (1.7)	0.057
White Cell Count ($\times 10^9/L$)	12.20 (10.00)	11.45 (9.23)	0.268
Neutrophil ($\times 10^9/L$)	6.40 (6.55)	5.65 (6.50)	0.169
Lymphocyte ($\times 10^9/L$)	3.0 (3.35)	3.2 (3.33)	0.469
Platelet ($\times 10^9/L$)	327.0 (203.0)	308.0 (206.5)	0.730

□ Mann Whitney Test

Clinical response after antimicrobial therapy:

During admission, antibiotics were prescribed for 100 (90.1%) children. The patients were treated with a wide range of antimicrobial regimens where they were generally classified into β -lactams monotherapy, macrolides monotherapy and the combination of a β -lactam plus macrolide.

Table-3: Clinical outcomes and antimicrobial therapy

Antibiotic	Cured	Failed	Total
Beta Lactam Mono	49 (76.6%)	15 (23.4%)	64
Beta Lactam Plus Macrolide	17 (94.4%)	1 (5.6%)	18
Macrolide Mono	18 (100%)	0 (0%)	18
Total	84	16	100

Sixty four patients received β -lactam monotherapy and 49 (76.6%) of them were cured (Table -111). On the other hand, only 18 patients received macrolide monotherapy which cured 100% patients. Although there was significant difference between three groups of regimen in term of efficacy ($p < 0.023$).

Discussion:

M. pneumoniae has been found to be an important infectious agent for the children’s pneumonia. In the present study 40.5% children had serological evidence of *M. pneumoniae* infection. Previous studies suggested that *M. pneumoniae* causes infection 20 – 35 % of children in Thailand, ⁶ Singapore.⁷ This variation might be due difference of study design and country.

Relating to clinical manifestation majority of our

patients presented with fever and cough. These are consistent with the previous studies which showed that fever and cough were the commonest presentation among patients with *M. pneumoniae* infection.⁸ On the contrary to previous studies; this showed that absence of cough would be more suggestive of *M. pneumoniae* infection. Other studies⁸ only included patients that were suspected of having either pneumonia, upper respiratory tract infection or both.

From the analysis, there was no association between duration of fever longer than six days and the serology result. However, previous study reported that the duration of fever in children with *M. pneumoniae* infection were likely to be longer as compared to those

without infection.⁹ This is probably due to the fact that 53.3% of our seropositive children are less than five years old.

The clinical signs studied in this research including tachypnoea, bronchial breathing and crackles were not found to have a significant association with serology results. Although another author⁹ demonstrated that crackles were more likely in *M. pneumoniae* infection; there were no other studies that supported this.

Study by Chen *et al.*¹⁰ showed significant association between *M. pneumoniae* infection with neutropaenia and thrombocytopenia where it was thought due to formation of antiplatelet and antineutrophil autoantibodies that caused the cytopaenias. On the other hand, an Australian study showed that patients with *M. pneumoniae* were more likely to develop thrombocytosis.¹¹ Our findings showed that laboratory findings are rarely diagnostic for *M. pneumoniae* and are not useful in therapeutic decision making.

In the present study sixty four patients received β -lactam monotherapy and 49 (76.6%) of them were cured. On the other hand, only 18 patients received macrolide monotherapy with 100% cured. Previous studies suggested that the use of macrolide should be considered for children admitted with community acquired pneumonia when *M. pneumoniae* was suspected.¹² However, β -lactam antibiotic was commonly started empirically when it was difficult to

diagnose *M. pneumoniae* based on initial clinical and laboratory findings before performing further diagnostic test for *M. pneumoniae*. The study showed treatment will reduce the morbidity of pneumonia and also reduce the duration of symptoms. These effects are seen more significantly with macrolide as compared to penicillin. Therefore, macrolide is still the antibiotic of choice as empirical treatment for children with CAP aged more than five years old when *M. pneumoniae* is highly suspected.

In conclusion, our results reemphasise that *M. pneumoniae* should be kept in mind as a cause of commu-

nity-acquired pneumonia of children in Malaysia. Although clinical parameters and laboratory findings have limited use of predicting *M. pneumoniae* infection, certain factors like age group and absence of cough may aid in deciding if the use of macrolide is needed.

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