

Prevalence of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in severe community-acquired pneumonia among hospitalized children in Iraq

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Abstract

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 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 November 2005 and March 2006. Serologic studies were performed for anti-*M. pneumoniae* and anti-*C. pneumoniae* IgM antibodies on admission using ELISA technique. Of 108 patients, 20 (18.5%) were seropositive for *Mycoplasma*, while 9 (8.3%) were seropositive for *chlamydia*, 2 (1.8%) were positive for a mixed infection and 106 (98.2%) were negative. The subjects' mean age was 4.1 months. *M. pneumoniae* infection was significantly increased with increasing of age, and highest percentage of infection (30.7%) was at age group 5-15 years ($p < 0.007$). *C. pneumoniae* infection was increased with increasing the age, and highest percentage of infection was (15.3%) at age group 5-10 years ($p = 0.157$). Our study suggests that *mycoplasma* and *Chlamydia* infections were commonly found among children hospitalized with severe pneumonia. Coverage with an appropriate antibiotic should be considered to hasten recovery.

Keyword: *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, community-acquired pneumonia

Introduction

Pneumonia is the most common cause of morbidity and mortality in young children worldwide [1,2], and the incidence is very high in developing countries [3]. 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 [4,5,6,7,8]. The findings from chest x-ray are different from clinical presentations. In recent years, *C. pneumoniae* has also been recognized as an increasingly common respiratory tract pathogen in both children and adults [7,11,12]. Patient age often determines the severity of the disease. *C. pneumoniae* can serve as a potent inflammatory trigger and can lead to an immunoglobulin E response. In addition, severe illness may affect previously healthy children and may result in complications such as pneumatocele, interstitial fibrosis or pneumothorax [13,14]. As a result of improved diagnostic techniques and provider awareness, we are now able to identify community-acquired pneumonia (CAP) more frequently. Severe CAP requiring intensive care unit (ICU) admission is a distinct entity with different pathogens, outcome and management [15]. However, the prevalence of *M. pneumoniae* and *C. pneumoniae* as a cause of severe pneumonia among hospitalized children has been rarely described [9]. Our objective in this study was to identify the prevalence of *M. pneumoniae* and *C. pneumoniae* in severe CAP among hospitalized children.

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. Patients were admitted to the Al-Mansoor Teaching Hospital for children's and Al-Kindy Teaching Hospital between November 2005 and March 2006. A total of 90 patients

with age ≥ 15 years, attended to the hospitals complaining diseases other than pneumonia, were examined as a control group. In general, a patient was enrolled in the study if he or she met the following criteria [16]: fever with body temperature ($>37.8^{\circ}\text{C}$), respiratory rate more than average per age by WHO criteria, a new pulmonary infiltrate evident on chest roentgenogram upon or within 24 hours of admission, sputum production, and abnormal chest examination findings (crackles or signs of consolidation). Patients were excluded if they were currently on 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* IgM antibodies using ELISA technique (PLATIA, Sanofi, Japan). Patients were positive for *C. pneumoniae* if their serum IgM was positive (presence of IgM $\geq 1/16$). The serological diagnosis was made if results were positive for anti-IgM titer $\geq 1/16$ in acute serum.

Statistical analysis: SPSS software (version 10) was used for statistical analysis. Significance of difference of the quantitative data was tested using analysis of variance test (ANOVA), while Chi-square (χ^2) was used for testing the significance of difference of the qualitative data. Odds ratio was used to measure the strength of association between two parameters. P value of < 0.05 was used as the level of significance.

Results and 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]. One hundred and eight infants and children were enrolled in the study from November 2005 to March 2006. Baseline clinical data are shown in Table 1. The mean age of the patients was 4.1 months (ranged, 1 month to 15 years). There were 55 (50.9%) males and 53 (49.1%) females. Anti- *M. pneumoniae* IgM were positive in 20 (18.5%) patients. Anti- *C. pneumoniae* IgM were

positive in 9 (8.3%) patients. In 2 (1.8%) of the patients, both anti-*M. pneumoniae* IgM and anti-*C. pneumoniae*

IgM were positive Table 2.

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

	<i>M. pneumoniae</i> No= 20		<i>C. pneumoniae</i> No= 9		P value
	No (+)	%	No (+)	%	
Sings ad symptoms	18	90	8	89	-
Cough	9	45	5	56	0.057
Sore throat	3	15	3	33	0.007
Hoarseness	11	55	4	44	0.077
Fever on examination (C)	10	50	6	67	0.081
Abnormal breath Sounds	5	25	3	33	0.022
WBC>10,000/c.mm	1	5	2	11	<0.0001
Hospitalization					

Table 2. Numbers and percentages of atypical pathogens detected in 108 infants and children's with pneumonia

Atypical pathogen	Number	%
<i>M. pneumoniae</i>	20	18.5
<i>C. pneumoniae</i>	9	8.3
Total	29	25

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% of CAP patients [6]. Further, a subgroup analysis in Thai children reported by Prapphal *et al.* [4] showed that *M. pneumoniae* was found in 14% and *C. pneumoniae* in only 3.4%. 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 25% of these children were positive either for *M. pneumoniae* or *C. pneumoniae*. The clinical presentations of atypical pneumonia was 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. This may be explained by their underlying illness [9].

Considering the clinical findings of the patients, Sore throat, Hoarseness, Fever on examination and Abnormal breath Sounds were found in 24 (22.2%), 6 (5.5%) , 15 (13.8%) and 16 (14.8%), respectively. Patients with *M. pneumoniae* (15%) were found to have less Hoarseness than those with *C. pneumoniae* (33%) ($p=0.007$). Patients with *M. pneumoniae* (55%) were with high fever on examination than those with *C. pneumoniae* (44%) but the difference did not reach statistical significance ($p=0.077$). Children infected with *C. pneumoniae* tended to have leukocytosis (leukocyte $\geq 10,000$ cells/ μ l),

compared to children infected with *M. pneumoniae* had significantly lower leukocyte ($<10,000$ cells/ μ l) ($P < 0.022$). The average length of hospitalization was at 2.6 days. The longest hospital stays were found in children with *C. pneumoniae* infection ($n = 2$; 10.2 days) ($P<0.0001$) Table 1.

Roles of *M. pneumoniae* and *C. pneumoniae* infection in hospitalized children were previously reported by Principi and Esposito [10], who found that 24% 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. In a recent study, Heiskanen-Kosma *et al.*, [18] showed that mixed chlamydial-mycoplasmal infections constituted 20% of *M. pneumoniae* infections and as many as 35% of *C. pneumoniae* infections. The important unanswered question in this regard is whether one pathogen simply facilitates the penetration of the other pathogen, or whether both truly cause pneumonia. Moreover, it is not known if the combination of *M. pneumoniae* and *C. pneumoniae* lead to a more sever clinical illness [19].

Table 3 shows that *M. pneumoniae* infection was increased with increasing the age, and highest percentage of infection was (30.7%) at age group 5-15 years ($p< 0.007$). *C. pneumoniae* infection was increased with increased the age, and highest percentage of infection was (15.3%) at age group 5-10 years ($p= 0.157$).

Table 3. Number and Percent of major etiologic agents detected in 108 infants and children's with pneumonia by age group.

Aetiological agent	< 5 years No =56		5 – 10 years No = 26		> 10 years No = 26		P value
	No	%	No	%	No	%	
<i>M. pneumoniae</i>	4	7	8	30.7	8	30.7	0.007
<i>C. pneumoniae</i>	2	3.5	4	15.3	3	11.5	0.157

In contrast, early population-based studies from the United States and Europe found that the incidence of *M. pneumoniae* and *C. pneumoniae* pediatric pneumonia was lowest among patients aged 5–15 years and highest among those aged 0–5 years [20]. This difference in age-specific incidence may relate to differences among study populations in the timing and frequency with which small children are exposed to other children. Although incidence was highest in the youngest age groups, the relative contributions of *M. pneumoniae* and *C. pneumoniae*

References

1. T. Heiskanen-Kosma, M. Korppi, C. Jokinen, *et al.* Etiology of childhood pneumonia: serologic results of a prospective, population-based study. *Pediatr. Infect. Dis. J.* 17(1998) 986-991.
2. M.N. Tsolia, S. Psarras, A. Bossios, *et al.* Etiology of community-acquired pneumonia in hospitalized school-age children: evidence for high prevalence of viral infections. *Clin. Infect. Dis.* 39(2004) 681-686.
3. B.A Cunha. The atypical pneumonias: clinical diagnosis and importance. *Clin. Microbiol. Infect.* 3(2006) 12-24.
4. N. Prapphal, S. Suwanjutha, P. Durongkaverroj, *et al.* Prevalence and clinical presentations of atypical pathogens infection in community acquired pneumonia in Thailand. *J. Med. Assoc. Thai.* 89(2006) 1412-1419.
5. F. Blasi, P. Tarsia, S. Aliberti, *et al.* *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. *Semin. Respir. Crit. Care Med.* 26(2005) 617-624.
6. M. Bamba, K. Jozaki, N. Sugaya, *et al.* Prospective surveillance for atypical pathogens in children with community-acquired pneumonia in Japan. *J. Infect. Chemother.* 12(2006) 36-41.
7. F. Blasi, P. Tarsia, S. Aliberti, *et al.* *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. *Semin. Respir. Crit. Care Med.* 26(2005) 617-624.
8. T.Q. Tan, J.R. Mason, W.J. Barson, *et al.* Clinical characteristics and outcome of children with pneumonia attributable to penicillin-susceptible and penicillin-nonsusceptible *Streptococcus pneumoniae*. *Pediatrics.* 102(1998) 1369-1375.
9. R. Samransamruajkit, S. Jitchaiwat, W. Wachirapaes, *et al.* Prevalence of *Mycoplasma* and *Chlamydia* Pneumonia in Severe Community-Acquired Pneumonia among Hospitalized Children in Thailand. *Jpn. J. Infect. Dis.* 61(2008) 36-39.
10. N. Principi, and S. Esposito, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* cause lower respiratory tract disease in paediatric patients. *Curr. Opin. Infect. Dis.*, 15(2002) 295-300.
11. J. Deerojanawong, N. Prapphal, S. Suwanjutha, *et al.* Prevalence and clinical features of mycoplasma pneumonia in Thai children. *J. Med. Assoc. Thai.* 89(2006) 1641-1647.
12. G. Liu, D.F Talkington, B.S. Fields, *et al.* *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* in young children from China with community-acquired pneumonia. *Diagn. Microbiol. Infect. Dis.* 52 (2005) 7-14.
13. M.H. Tsai, Y.C. Huang, C.J. Chen, *et al.* Chlamydial pneumonia in children requiring hospitalization: effect of mixed infection on clinical outcome. *J. Microbiol. Immunol. Infect.* 38(2005) 117-122.
14. Martin, R.J. Infections and asthma. *Clin. Chest Med.* 27(2006) 87-98.
15. N. Dahmash, and M. Chowdhury, Re-evaluation of pneumonia requiring admission to an intensive care unit: a prospective study. *Thorax*, 49(1994) 71-76.
16. World Health Organization: Technical bases for the WHO recommendation for the management of pneumonia in children at first level health facilities. World Health Organization, Geneva (1991).
17. J. Hietala, M. Uhari, H. Tuokko, *et al.* Mixed bacterial and viral infections are common in children. *Pediatr. Infect. Dis. J.* 8(1989) 683-686.
18. T. Heiskanen-Kosma, M. Korppi, A. Laurila, C. Jokinen, M. Kleemola, P. Saikku, *Chlamydia pneumoniae* is an important cause of community-acquired pneumonia in school aged children: serological results of a prospective, population-based study. *Scand. J. Infect. Dis.* 31(1999) 255-259.
19. S. Esposito, F. Blasi, F. Bellini, *et al.* *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* infections in children with pneumonia. *Eur. Respir. J.* 17(2001) 241-245.
20. A.R. Gonzalez, M. Falguera, A. Nogues, M. Rubio-Caballero, Is *Streptococcus pneumoniae* the Leading Cause of Pneumonia of Unknown Etiology? A Microbiological Study of Lung Aspirate in Consecutive Patients with Community-acquired Pneumonia. *Amer. J. of Med.* 106 (1999) 358-390.
21. J.A. Harris, A. Kolokathis, M. Campbell, G.H. Cassell, M.R. Hammerschlag, Safety and efficacy of azithromycin in the treatment of community-acquired pneumonia in children. *Pediatr. Infect. Dis. J.* 17(1998) 865-871.
22. N. Principi, S. Esposito, F. Blasi, L. Allegra, Role of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in children with community-acquired lower respiratory tract infections. *Clin Infect Dis.* 32(2001) 1281-1289.
23. C.R. Phares, P. Wangroongsarb, S. Chantra, W. Paveenkitiporn, R.F. Tondella, Benson, *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.* 45(2007) 147-155.

انتشار ذات الرئة النمطية الحاد المتسبب بجراثيم المايكوبلازما الرئوية و الكلاميديا الرئوية بين الأطفال

المُدخلون للمستشفى في العراق

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الملخص:

ذات الرئة النمطية تعتبر من أكثر الأمراض التي تصيب الأطفال وتسبب هلاكات واسعة حول العالم، وتشكل جرثومة المايكوبلازما الرئوية و الكلاميديا الرئوية السببان المرضيان الشاذان الأكثر شيوعاً كمسببان للاصابة. هذه الدراسة صُممت لتحديد انتشار ذات الرئة الحاد المتسبب عن طريق الاصابة بالمايوبلازما و الكلاميديا في الأطفال الذين أدخلوا للمستشفى. حيث اشتملت هذه الدراسة على 108 مريض بعمر 15 شهر الى سنة ادخلوا للمستشفى للفترة الممتدة من شهر نوفمبر 2005 الى شهر آذار 2006، لانهم يعانون الاعراض السريرية التالية : حمى بدرجة حرارة اكبر من 37.5 درجة سلزية، ارتفاع معدل التنفس عن الحد الطبيعي وجود ارتشاح رئوي جديد وواضح على الصدر في اول 24 ساعة من الدخول، إنتاج لعاب، ونتائج فحص صدر شاذة أو وجود اصوات خشخشة في الصدر. المرضى الذين إستثنوا من هذه الدراسة الذين تم علاجهم بالمضادات الحيوية أو أدخلوا إلى المستشفى لأكثر من 48 ساعة. اجريت دراسة سيولوجية للكشف عن الازداد نوع IgM الخاصة بالمايوبلازما و الكلاميديا باستخدام تقنية الاليزا . بالنسبة لل 108 مريض الذين ادخلوا في هذه الدراسة، نتيجة 20 (18,5%) منهم كانت إيجابية لاضداد المايكوبلازما الرئوية ، و 9 (8,3%) كانت إيجابية للكلاميديا الرئوية، فقط 2 (1,8%) كانت إيجابية للاصابة الخلطية المشتركة. الاصابة بالمايكوبلازما الرئوية كانت تزيد بشكل ملحوظ بزيادة العمر، وان اعلى نسبة مئوية من الاصابة كانت (30,7%) في المجموعة العمرية 5-15 سنوات ($p < 0.007$). اما الاصابة بالكلاميديا الرئوية كانت تزيد بزيادة العمر، وان اعلى سبة مئوية للاصابة كانت (15,3%) في المجموعة العمرية 5-10 سنوات ($p = 0.157$). هذه الدراسة اظهرت بأن الاصابة بالمايكوبلازما الرئوية و الكلاميديا الرئوية وجدت بنسبة معنوية لدى الأطفال الذين أدخلوا المستشفى نتيجة الاصابة بذات الرئة الحاد. وان استخدام المضادات الحيوية ضروري ويجب أن يؤخذ بنظر الإعتبار لتعجيل الشفاء من الاصابة.